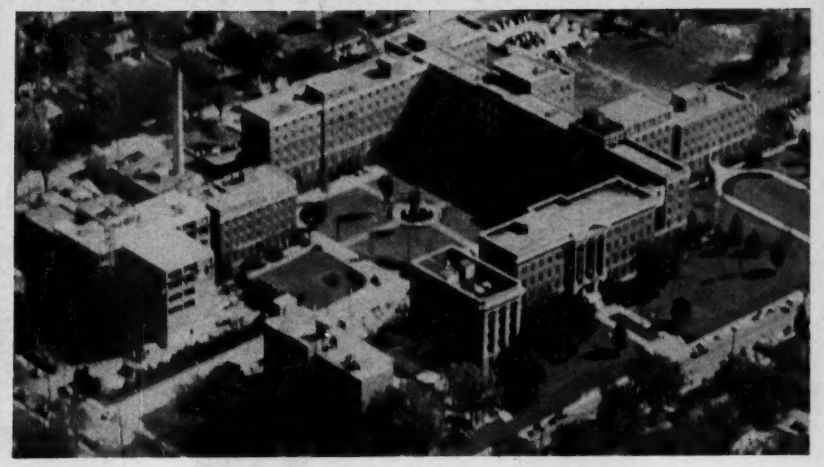
The Journal

OF THE KANSAS MEDICAL SOCIETY



UNIVERSITY OF KANSAS MEDICAL CENTER

Seventh Annual University of Kansas School of Medicine Number

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March, 1953 Vol. LIV, No.3

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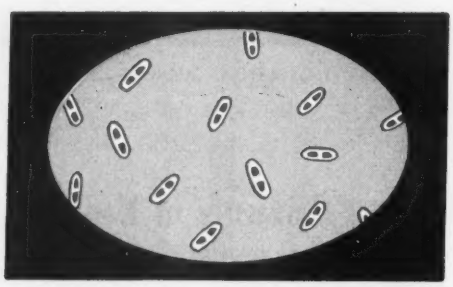
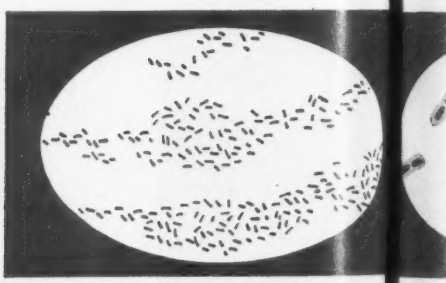
notably effective

well tolerated

broad spectrum antibiotic . . .





highly effective in a wide range of bacterial, rickettsial, and viral pneumonias, CHLOROMYCETIN (chloramphenicol, Parke-Davis) is particularly valuable in mixed infections and where the causative agent is not easily ascertained.

unusually active against staphylococci CHLOROMYCETIN reduces the likelihood of bronchopulmonary staphylococcal superinfection, an increasingly common complication.

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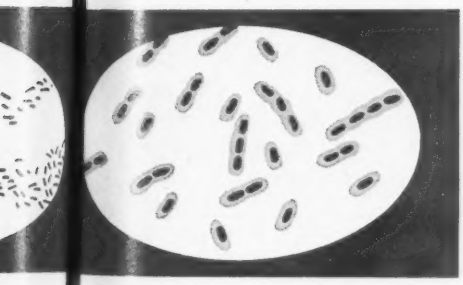
in the pneumonias



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Curbstone Consultation

ADENOMATOUS POLYPS OF THE COLON AND RECTUM: In a study of 234 patients with polyps, associated cancer of the colon was found in 36% of the group. However, 2/3 of the growths were within the reach of a 25 cm. sigmoidoscope. In the same group, more than one polyp was found in 33% of the patients. Thus, the finding of a single polyp should certainly indicate further examination of the large bowel.

DeMuth, W. E. et al: Adenomatous Polyps of the Colon and Rectum, Surg., Gynec. & Obst. 94:195 (Feb.) 1952

Pathologically Speaking

TRANSUDATES AND EXUDATES

THE ABNORMAL accumulation of fluid in joints, cerebrospinal canal, body cavities and subcutaneous tissue often is encountered by the physician.

It is of importance for the physician to establish the cause of these abnormalities in order that prevention and proper therapy may be instituted. It is also important to establish whether the accumulated fluid is a transudate or an exudate. Separating the fluid into one of two general classifications will aid in the clinical approach to the existing problem.

The separation of fluids into transudates and exudates is at times easy; however, overlapping frequently occurs.

Transudate:

1. Usually clear and colorless
2. Does not clot
3. No fibrinogen
4. Low specific gravity (1.010 ± 0.003)
5. Low protein content (0.4 ± 0.2 gm./100 c.c.)
6. Contains few cells, usually lymphocytes and red blood cells.
7. Sterile, unless contaminated in collection

Exudate:

1. Usually cloudy or turbid
2. Usually will clot
3. Fibrinogen present
4. Specific gravity usually over 1.020
5. Protein usually elevated and will approximate the levels of blood
6. Many cells present, depending upon etiology
7. Organism may be identified

Transudates may be associated with the following conditions:

1. Circulatory failure
2. Venous obstruction
3. Cirrhosis of the liver
4. Disease producing hypoalbuminemia
5. Nephrosis
6. Retention of sodium

Exudates may be seen in the following:

1. Infections
2. Trauma
3. Neoplastic disease

The evaluation of abnormal collection of fluid is of importance and should be thoroughly investigated for correlative or diagnostic impressions.

RALPH EMERSON DUNCAN, M. D.
LORAINE E. SCHULTZ, M. D.
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1. Reich, W. J., et al. (1952), A Recent Advance in Estrogen Therapy. II. American J. Obst. & Gynec., 64-174, July

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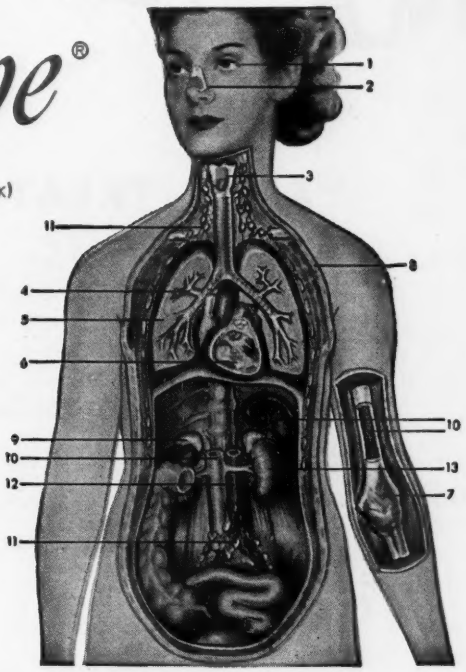

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Anatomy *of the* Mouth

1. Olfactory nerve
2. Anterior ethmoidal artery
3. Ophthalmic nerve
4. Maxillary nerve
5. Sphenopalatine ganglion
6. Anterior, middle & posterior superior alveolar nerves
7. Maxillary lymph nodes
8. Anterior palatine nerve
9. Great palatine artery
10. Buccinator lymph nodes
11. Lingual nerve
12. Inferior alveolar nerve & artery
13. Lingual artery & vein
14. Mylohyoid nerve & artery
15. Supramandibular lymph nodes
16. Submental lymph nodes
17. Submaxillary lymph nodes
18. Trachea
19. Sensory root of trigeminal nerve
20. Motor root of trigeminal nerve
21. Superficial temporal artery & vein
22. Mandibular nerve
23. Sphenopalatine artery
24. Internal maxillary artery
25. Parotid lymph nodes
26. External carotid artery
27. Pterygoid venous plexus
28. Oropharynx
29. Anterior & posterior facial veins
30. External maxillary artery
31. Hypoglossal nerve
32. Vagus nerve
33. External jugular vein
34. Internal carotid artery
35. Esophagus
36. Internal jugular vein

This is one of a series of paintings by Paul Peck, illustrating the anatomy of various organs and tissues of the body which are frequently attacked by infection, where aureomycin may prove useful.

Lederle

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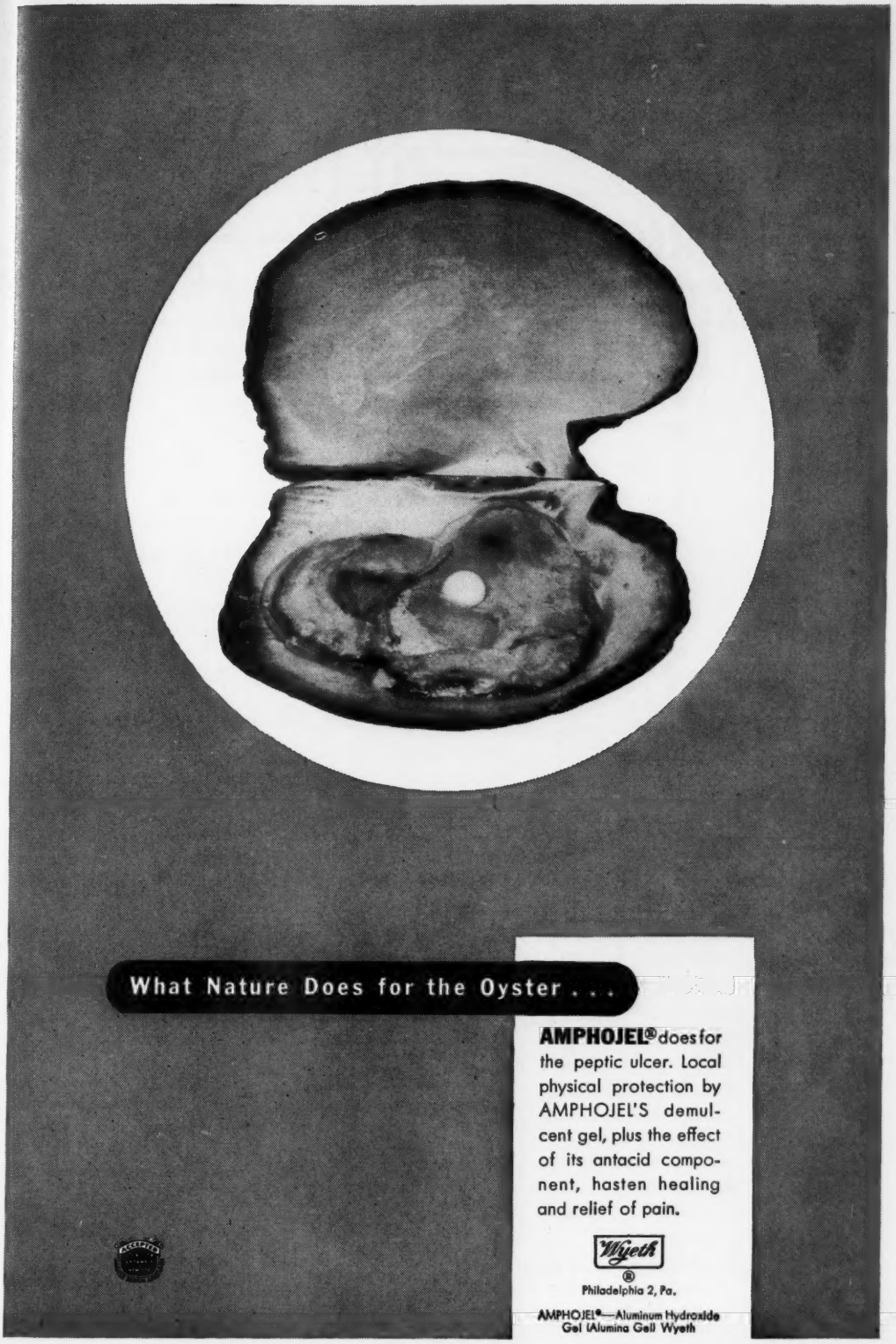
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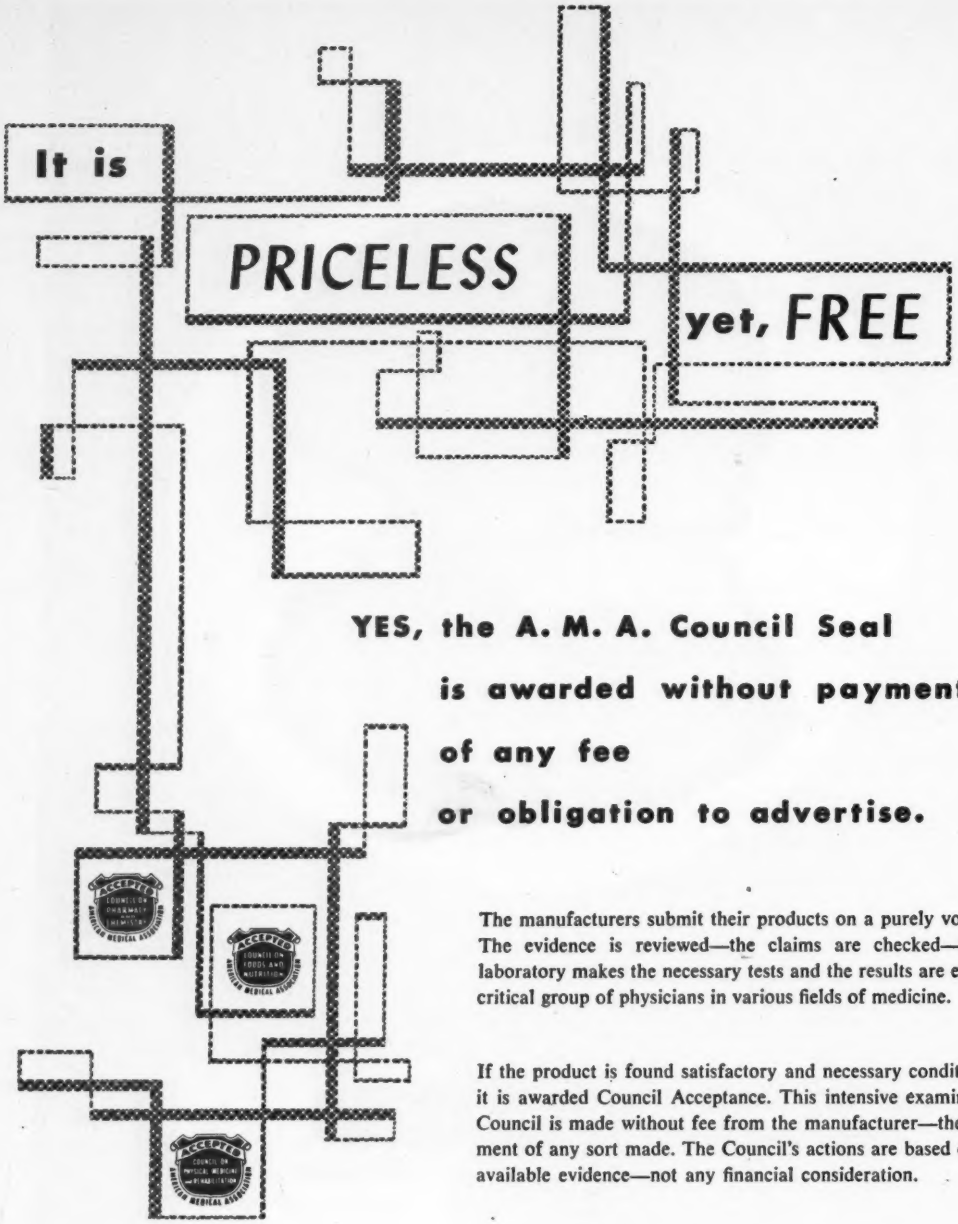

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Meat occupies a prominent position in the weight reduction diets outlined in this American Heart Association booklet. This recommendation is in sharp contrast to the erroneous belief held in former years that meat is harmful in hypertension or cardiac disease. "There is no evidence that red meat or any other form of protein in moderation has any adverse influence on blood pressure."

The magic formula for reducing is simply "Eat less." Two types of diets are outlined. One "allows moderate amounts of meat and other proteins, small amounts of fat and moderate amounts of carbohydrates." The other is "high in protein with plenty of meat, eggs and cheese, moderate in fat and low in carbohydrates." Diet No. 1 provides 70 Gm. of protein, 60 Gm. of fat, and 120 Gm. of carbohydrate; caloric yield, 1,300. Diet No. 2 provides 100 Gm. of protein, 80 Gm. of fat, and 60 Gm. of carbohydrate; caloric yield, 1,360.

The inclusion of generous amounts of meat in these diets—12 to 16 ounces of cooked meat or two substantial servings each day in Diet No. 2—is a reflection of the important role meat plays in any weight reduction regimen. It is generously included because of its high content of protein of excellent biologic value and because lean meat contains unobjectionably small amounts of fat.

*Food For Your Heart, a Manual for Patient and Physician, Department of Nutrition, Harvard School of Public Health, Harvard University, The American Heart Association, Inc., New York, 1952. Copies available through local Heart Association.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

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CHEVALIER L. JACKSON, M.D., Professor of Laryngology & Broncho-Esophagology, Temple University School of Medicine, Philadelphia.

DANIEL B. KIRBY, M.D., Professor of Ophthalmology, New York University; author, "Surgery of Cataract."

KINSEY M. SIMONTON, M.D., Associate Professor of Otolaryngology, The Mayo Foundation & University of Minnesota Graduate School.

FRANCIS A. SOOY, M.D., Associate Professor of Otolaryngology, University of California, San Francisco.

FRANK B. WALSH, M.D., Associate Professor of Ophthalmology, Johns Hopkins University, Baltimore.

BYRON J. ASHLEY, M.D., Ophthalmologist, Topeka.

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April 13 to 15, 1953

Guest Instructors:

JOHN ADRIANI, M.D., Clinical Professor of Surgery (Anesthesiology, Louisiana State University; Professor of Surgery (Anesthesiology), Tulane University, New Orleans.

VIRGINIA APGAR, M.D., Associate Professor of Anesthesiology, Columbia University, N. Y.; Chairman, American College of Surgeons.

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HAROLD R. GRIFFITH, M.D., Professor of Anesthesiology & Chairman of Department, McGill University, Montreal.

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LAWRENCE F. SCHUMACHER, JR., M.D., Professor of Anesthesiology, Baylor University; Director of Anesthesiology, Hermann Hospital, Houston.

GEORGE J. THOMAS, M.D., Professor of Surgery & Chairman, Section of Anesthesiology, University of Pittsburgh; Research Associate, Explosives Division, U. S. Bureau of Mines; Chairman, Committee on Hospital Hazards & Standardization of Anesthesia & Resuscitation Equipment, A. S. A.

JOHN GILROY, Ph.D., Manager, Equipment Development & Research, Ohio Chemical & Surgical Equipment Company, Madison, Wisc.

HEMATOLOGY

April 23 to 25, 1953

Guest Instructors:

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Anesthetic in Hospital	10.00	20.00	30.00	40.00
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Medicines in Hospital	10.00	20.00	30.00	40.00
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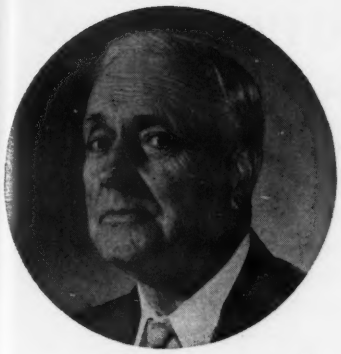

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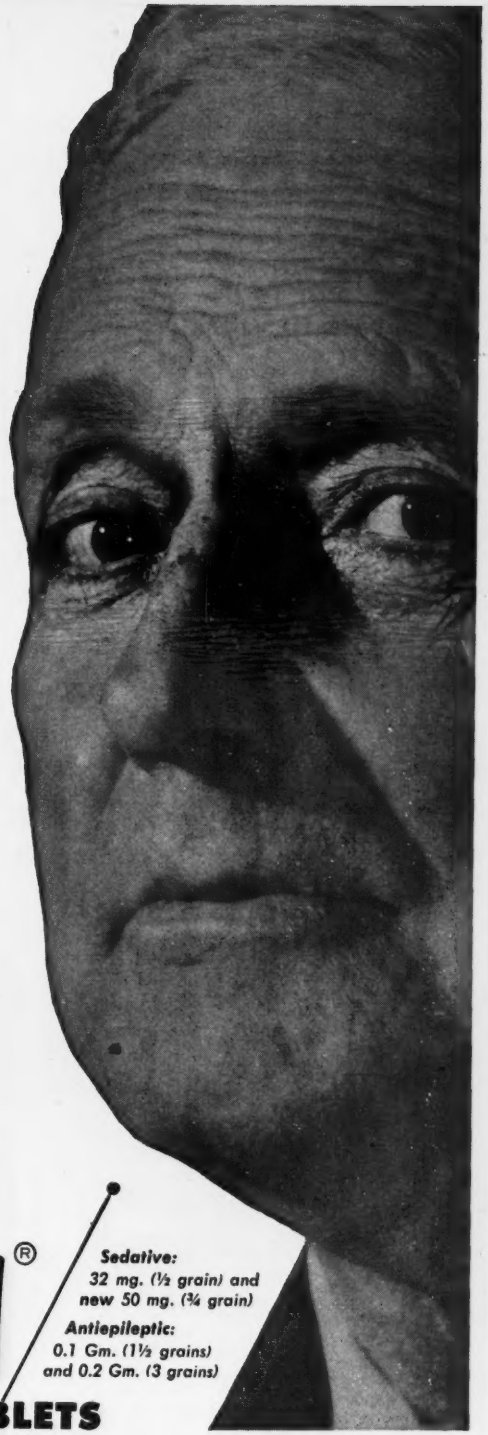

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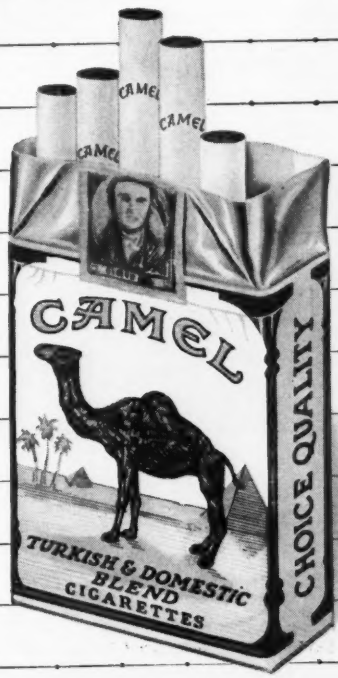

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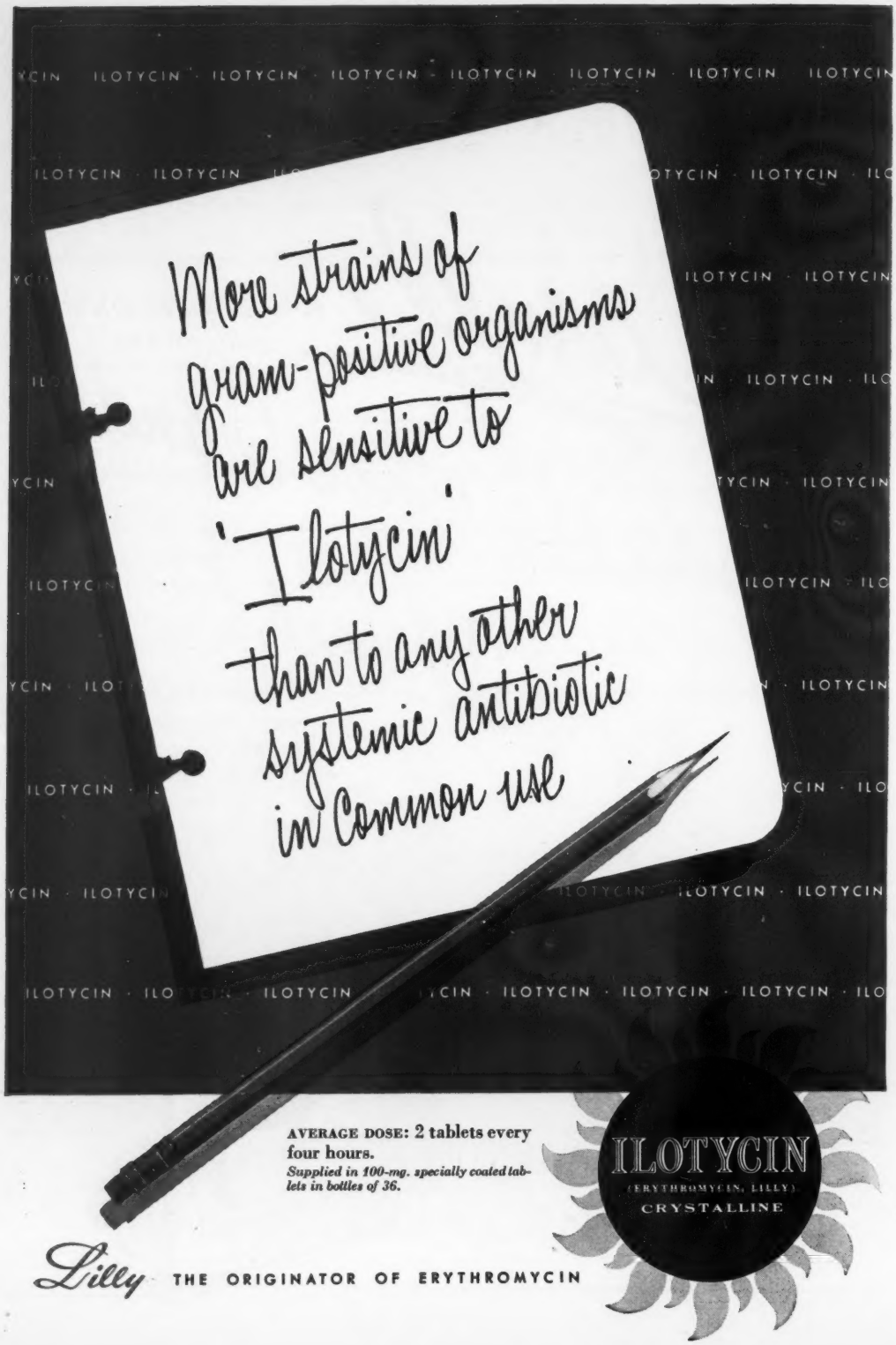
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Greetings!

It is a pleasure to be able to introduce to the members of the Kansas Medical Society the annual medical school issue. Originally it had been intended that my report on the progress of your school would be included in this issue. For practical reasons that report appeared in the preceding issue; I believe that the accomplishments described therein reflect great credit on the Society and every Kansas physician.

Your Committee on Medical Schools has taken an active interest in the school this year. During the course of two excellent meetings, several suggestions were made for articles to be published in the Journal. One of these articles, relating to medical school admission policies, will be ready for an early issue. I would hope that members of the Society feel free to request certain articles of general interest from the administrative officers or faculty of the school. Only in this way can we serve you best.

W. CLARKE WESCOE, M.D., Dean
University of Kansas School of Medicine

Treatment of Cervical Stump Carcinoma

Galen M. Tice, M.D.*

Kansas City, Kansas

A review of cases of carcinoma of the cervix treated in the Department of Radiology of the University of Kansas School of Medicine during the period of 20 years from January, 1933, to January, 1953, was recently made. In this interval, 240 cases of carcinoma of the cervix came to our observation for treatment. These cases were exclusive of those cases in which the treatment was shared by some other physician. In this series of cases we found 26 cases of carcinoma of the cervical stump.

In reviewing the literature on the subject of carcinoma of the cervical stump, we find considerable stress placed by gynecologists on the time interval that has elapsed since the removal of the uterus and the discovery of carcinoma in the cervix. Donnelly and Bauld[5] express the opinion of most authors as follows: "We classify true stump cancer as those cases in which malignant lesion is diagnosed two or more years after the subtotal hysterectomy. . . . The problem of the stump cancer under two years is essentially one of missed diagnosis, whereas the true stump cancer may be considered the result of inadequate surgery for benign conditions."

Meigs[12] suggests that carcinoma missed at the time of hysterectomy, "is due to lack of inspection and examination of the cervix at the time of operation. It is probable that the patients were bleeding and had fibroids, and that the abdominal operation was done and the uterus removed without preliminary inspection of the cervix in the lithotomy position. In other cases the cancer develops within three to six months postoperatively and was certainly present at the time of the operation, but was not recognized because it was so early or was present in the endocervix."

Witte and Ovitt[26] would divide cervical stump carcinoma into three groups. Group 1 would include those that occurred during the first year following supracervical hysterectomy. Group 2 would be that series of cases diagnosed in the second and third year. Group 3 would include those cases occurring three years after supracervical hysterectomy. The last group would represent the cases that in their opinion should be called "true primary" stump carcinoma. Group 1 would represent the case in which tumor was surely present at the time of surgery, and Group 2 would include the cases in which the tumor was probably present at the time of removal of the uterus.

Ward[23] suggested one year as the proper time after supracervical hysterectomy to classify the cervical carcinoma as a "true stump" carcinoma. Van Graef[22] favored two years instead of one. Nuttall and Todd[15] agreed with Van Graef. Healy and Arneson[8] present evidence of long duration of cancer of the cervix before diagnosis, and they chose three years as the time interval.

Meigs,[11] in 1936, reported 80 cases of carcinoma of the cervical stump from records of Massachusetts General Hospital and from Massachusetts State Cancer Hospital. Of these, 32 were cancer of the vaginal vault occurring after panhysterectomy. Twenty-three cases occurred within one year and were considered to be cases in which tumor was present at the time of hysterectomy. In nine cases, adenocarcinoma had been diagnosed in the uterus at the time of hysterectomy, and adenocarcinoma found in the cervix was considered to be a recurrence. Only 21 cases classified as "real stump cancer" were recorded. He found, then, only 2.1 per cent of true stump cancers.

Our 26 cases of cervical carcinoma were divided as to the time interval between diagnosis and the supracervical hysterectomy as follows:

Less than 6 months	9 cases	35% of series
½ to 2 years	4 cases	15% of series
2 to 5 years	4 cases	15% of series
5 to 22 years	9 cases	35% of series

For the purpose of comparing with statistics where only the "true" carcinoma of the stump is considered, 50 per cent of our cases would fall into the latter group and the other half would be in that group where tumor was found within the two-year interval that seems to be accepted by most gynecologists.

It seems to us, as radiologists whose primary interest is in the treatment of the case, that whether the tumor was present before hysterectomy or whether it developed as a separate primary tumor later, is of academic interest. When the case is referred to us for radiation therapy, we must adjust to the immediate situation without worrying about the historical events leading to the diagnosis. A distinctly different treatment problem presents itself than in the case of the carcinoma of the cervix in which the uterus has been retained. Perhaps this attitude is too isolated. The radiologist who sees 50 per cent of his stump cancers of the type that should have been

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diagnosed at or before hysterectomy, has an obligation in joining his gynecologist colleagues in urging the surgeon who handles these cases to cut around and not through the cancer.

It is not my province to judge whether the surgeon should do a supracervical or a complete hysterectomy in each case. It is interesting to review the remarks of leading gynecological surgeons in this respect. Ward,[23] in 1941, said, "In my opinion the total operation is to be preferred and is my present practice because of the evident higher incidence of stump cancer than was formerly thought to occur and of the frequent association of cancer with fibroids. Yet we must recognize that in average hands there is more danger of a higher mortality and such complications as injury to the bladder and rectum, infection and lack of vaginal support, than in skilled hands. Also the expert surgeon will meet cases with a definite increase in risk due to obesity, adhesions, fixation or systemic disease, which makes the subtotal operation a safer and wiser procedure. If, however, the subtotal is considered, a careful study of the cervix should be made and appropriate treatment used if indicated."

Ward mentioned vesicovaginal fistula as a complication that occurred one and a half times as often when the complete operation was done, as compared to the partial procedure. Behney[1] considered this also as an added risk. The difficulty in applying a capsule of radium was mentioned as the reason for this added risk.

Masson,[10] in 1940, said, "For the occasional operator or for the surgeon who has not taken special pains to become thoroughly familiar with the technique of total abdominal hysterectomy, my advice would be to continue doing the subtotal operation in a large majority of his cases, even at the risk of having an infected cervix which might require treatment or removal at a later date. A neglected infected cervix is a definite predisposing cause for complications. The most frequent of these is thrombophlebitis, and the gravest are pulmonary emboli and the later development of cancer."

Perhaps the most logical and accurate method of evaluating the added risk, if such there is, in doing a complete hysterectomy, as compared to supravaginal hysterectomy, is to compare the mortality figures. The figures submitted below are from large medical centers and perhaps do not reflect the mortality in the hands of the less skilled surgeon.

Meigs[11] reviewed reports from eight clinics in which surgery occurred prior to 1936. This included 2,003 complete hysterectomies with a primary mortality of 4.07 per cent and 7,945 supracervical hysterectomies with a mortality of 1.6 per cent. The report by Meigs was made prior to the use of antibiotics, and perhaps the blood bank was not used as efficiently as in later reports. Actually the figures in Table 1 do not indicate a great deal of added risk for complete hysterectomy as compared to supracervical hysterectomy.

TABLE 1
COMPARATIVE MORTALITY RATES

Surgeon		*Supravaginal Hysterectomy*	*Complete Hysterectomy*
Masson, Mayo Clinic—1940	(10)	0.9%	1.2%
Te Lind—1941	(20)	0.15%	0 %
Witte and Ovitt—1951	(26)	0.65%	0.57%
Reed and Bell—1933	(17)	2.1%	3.1%
Jones and Doyle—1943	(9)	1.43%	1.05%
Waters—1942	(25)	1.9%	0 %
Phillips—1945	(16)	....	0.46%

Other potential reasons for leaving the cervix are discounted by most surgeons. Among these are mentioned the need of support for the vagina and the danger of foreshortening the vagina. The danger of infection of the stump as a distinct hazard, separate from the possibility of cancer, is stressed by Tyrone and Weed.[24]

Cell type, as in carcinoma of the cervix as a group, was in our group predominantly squamous cell carcinoma. The pathology was divided as follows:

TABLE 2
PATHOLOGY

Squamous Cell Carcinoma	19 cases
Plexiform Carcinoma	1 case
Adenocarcinoma	6 cases

Three of the cases in which adenocarcinoma of the cervix was diagnosed had subtotal hysterectomy within two months prior to the recognition of the cervical carcinoma. In each case, carcinoma of the uterus was diagnosed at surgery. These three cases are living following treatment, 4½ years, 4 years, and 3 months, respectively. In another case where adenocarcinoma of the cervix was diagnosed, history indicated that the uterus had been removed 22 years before. I doubt that any conclusion can be drawn from the cell type, except in the case where adenocarcinoma is diagnosed within less than two years after subtotal hysterectomy. This would suggest primary carcinoma of the uterus with extension or recurrence in the cervix.

Most authorities consider it impossible to determine the incidence of stump carcinoma where the uterus has been removed, as compared to a similar number of cases where carcinoma develops in the cervix in the woman who still has her uterus. It would be impossible to know which cases of operated women to select for the control group, since, as in one of our cases, the carcinoma developed 22 years after hysterectomy. An attempt has been made to correlate the number of stump cancers to the number of cervical carcinomas seen in the woman who has not had a hysterectomy. Table 3 lists the

TABLE 3

COMPARATIVE INCIDENCE OF STUMP CARCINOMA AND ALL CARCINOMA OF THE CERVIX: FIVE-YEAR SURVIVAL OF STUMP CARCINOMA

Author	*Number of Cases of Carcinoma of the Cervix*		*5-year Survival of Carcinoma of the Cervix*	*Incidence of Stump Carcinoma*	*5-year Survival of Stump Carcinoma*
Masson	(10)				20.0%
Ward and Sackett	(27)	879	28.5%	6.9%	42.8%
Scheffey	(18)	369	15.8%	4.8%	41.6%
Healy and Arenson	(8)	2,600	24.0%	2.6%	14.0%
Costlow	(4)	2,071		4.9%	32.5%
Donnelly and Bauld	(5)	780		5.1%	15.0%
Van Graef	(2)			4.1%	
Our figures		240	(All cases)	10.8%	23.0%
			(True stump)	5.4%	

relationship between the two types of cervical carcinoma and records the five-year survival as listed by several authors. Our record is included in the table. It is not clearly recorded in the various reports whether the figures given are for "true" stump carcinomas or all stump carcinomas. Since our interest in this paper is primarily in treatment, we have lisfed all of ours. Our ratio of total stump carcinomas to our entire group is 10.8 per cent. If we would consider only the 13 cases that occurred two years after supravaginal hysterectomy, our "true" stump cases, our figure would be 5.4 per cent, which approaches the figures given by others.

In our series, 12 are living and 14 are dead. The average length of life of those dead was 2.5 years. This includes two patients who lived one and two months respectively. These cases were moribund when first seen. Treatment was by external radiation only in an attempt to control bleeding and pain. It also includes two patients who lived six years each. One of these patients died of a cerebral accident, and one died following abdominal surgery for a carcinoma of the hepatic flexure of the colon, her second primary tumor. Both were free from evidence of stump carcinoma at death. Twelve of the patients are living, and seven have lived beyond the five-year period. This constitutes 23 per cent five-year survival in our small series. One patient is living ten years with no demonstrable disease. Another case was considered so far advanced when first seen that x-ray therapy was given externally as a palliative procedure, through external ports only. Two additional series have been given since her first treatment. She is now living, eight years with disease but in fair comfort.

Radiation therapy is recognized as the treatment of choice in stump carcinoma, as in the case of cervical carcinoma that has not had uterine surgery. Where radium is used to control the local lesion, various techniques are used. It is generally agreed that placement of a radium applicator in contact with a shallow cervical stump, and keeping it accurately in contact with the disease, is a difficult and sometimes inaccurate procedure. Unless the operation was a subtotal hysterectomy, there will be no chance to use a T or Y applicator. A plaque or mold containing radium capsules may be packed in place. Maintaining good contact for a long period of time will depend on careful packing of the vaginal vault.

Radium therapy may be hazardous. It is generally recognized that, because of the proximity of the bladder which may be used to cover the stump, or because of gut that may be plastered to the stump area, a smaller dose should be used than is used in uncomplicated carcinoma of the cervix. Witte and Ovitt[26] use 1,800 millicurie hours of radium. They do not indicate the length, shape or filtration of the units used. This is followed by external roentgen therapy and a second application of 1,800 millicurie hours of radium. Costlow[4] makes repeated applications of radium using 50 or 75 mg., supplemented by external roentgen therapy. Skinner[19] has for many years advocated implantation of small, low-intensity radium needles into the carcinoma, supplementing this with external radiation.

Meigs[12] emphasizes the difficulty of applying radium because the canal of the cervix cannot be used as the source of a central radium applicator. He considers the danger of fistula formation greater because of the lack of a protecting uterus. He does not designate his treatment choice but indicates that in some clinics a vaginal cervicectomy is done in early cases of carcinoma of the stump. He believes that if surgery is to be done it should consist of the Wertheim operation with removal of nodes and vaginal tissue.

Ward[23] treats the cervix with a radium capsule and 12.5 mg. radium needles implanted in the periphery for a total dose of 3,200 to 3,600 mg. hours.

Our treatment schedule has varied over the 20-year period. In every case we have supplemented the treatment of the local lesion with roentgen therapy. Both our external therapy technique and our intravaginal radiation have changed. We have attempted in the past to treat the local lesion with radium applied to the surface. In a few cases we have supplemented this with needles. For the last eight years we have been using intravaginal or, perhaps a more accurate

term, transvaginal therapy. Of the cases not now living, four were treated with transvaginal radiation and six with radium, and four were so far advanced that external radiation only was used. The living cases were treated as follows: One case had external radiation only, two were treated with radium, and nine were treated with transvaginal radiation. In this later series the dose varied from 5,000 r to 10,000 r, measured in air with an average dose for the series of 7,000 r.

It is our plan to treat all cases of carcinoma of the cervical stump by transvaginal radiation. Intravaginal radiation was advocated by Merritt[13] in 1920. Erskine[7] has advocated its use for years. Erskine, and Merritt and his associates have designed special applicators for this type of treatment. Buslog,[3] Elkins,[6] and Wasson[24] have been among those advocating transvaginal radiation. Behney,[1] in his report in 1940, says in referring to treatment of stump carcinoma, "Per-vaginal high voltage x-ray therapy was employed in one of our recent cases, as well as for more than 50 cases of ordinary cancer. *This form of irradiation seems peculiarly adapted* for safe and thorough radiation of cancerous cervices after the fundus has been removed."

We agree with Nolan and Stambro[14] that the one-field treatment plan for transvaginal roentgen therapy is limited as to dosage by the reaction at the level of the external os. A maximum amount of 10,000 r is their accepted dose. We have not at any time gone beyond this limit with a one-field technique. They feel that if a one-field technique is used the result should be as efficient as when radium alone is used. We have felt, in treating all types of carcinoma of the cervix, that transvaginal radiation has something to offer when a large, bulky, fungating tumor is present. When it was felt, in cases of cervical carcinoma, that destruction of this bulky tumor might make access to the canal easier for later radium insertion, we have rather routinely used the transvaginal port.

If the treatment is of primary carcinoma of the stump of the cervix, it seems that the problem is much the same as in treatment of a lip cancer. We attempt to destroy the primary tumor with a big dose of radiation directed at the tumor, and we depend on external ports for radiation of the parametria. We recognize the possible value of angling the tube as much as 30 degrees to irradiate the adjacent parametria, as described by Bond[2] and others. Up to the present, we do not feel that we can do angle ports on all sides of the cervix efficiently and accurately. We are still trying. Up to now we use a single port of from 7,500 r to 10,000 r air dose directed at the cervix.

Our present technic uses H v 1 of 1.0 to 1.5 mm. of copper, depending on the bulk of the tumor to be treated. We use the largest bakelite speculum that will be accommodated by the vagina. A metal tube to fit the speculum columnates the ray up to the vaginal orifice. Our cones measure from 2.0 to 3.5 cms. in diameter. The ray spreads from entrance at the vaginal orifice, depending on the size of the metal tube. We give from 500 r to 750 r daily through the transvaginal port. On the same day the patient gets two external ports crossfiring the pelvis. We expect our treatment series to be given in 20 sessions. External ports consist of two ports anterior to the pelvis and two ports posteriorly. If the patient is large and we are afraid of excess skin damage, we do not hesitate to use lateral and perineal ports. We attempt to deliver a depth dose of 2,400 r to the mid parametria.

The rationale of transvaginal therapy for stump carcinoma seems to us to be quite obvious. We use a divided dose as compared to the relatively undivided dose when radium is used. It is granted that if radium is used, it should be given in two or three separate applications. When transvaginal x-ray is used, there may be as many as 20 separate applications. When radium is used, it is possible that a coil of gut, even though not plastered down close to the radium, may lie more or less inert adjacent to the radium, and be overradiated. With numerous applications of small doses of x-ray, this same segment of gut would hardly be overradiated. If the bladder or gut is plastered to the peritoneal side of the stump, in either instance there will be heavy radiation, but the repeated doses will permit some degree of recovery of the damaged normal tissues that will not be possible if a massive dose of radium is applied. A relatively minor advantage in transvaginal radiation is the fact that the patient can be handled as an outpatient. The expense of a hospital bed, operating room, and anesthetic are avoided. If the patient develops side effects such as nausea and diarrhea, we merely stop treatment for a few days. We do not feel that we must push the treatments rapidly, as we might if the patient were paying for a hospital bed.

The figures of Ward, Scheffey, and Costlow (Table 3) would indicate that salvage of stump carcinoma is as good as, or better than, that in the case of cervical carcinoma where the uterus has not been removed. Meigs[12] reports a summary of 5,672 cases of carcinoma of the cervix, seen in nine clinics. These cases showed a five-year survival rate of 26.3 per cent. Donneley and Bauld's figures and Healy and Arneson's figures fall below this level in treatment of the stump case. Our figure of 23 per cent is a little less than the over-all figure of 23.6 per cent quoted by Meigs.

SUMMARY AND CONCLUSIONS

1. In 20 years we have handled the complete treatment, not including surgery, of 240 cases of car-

cinoma of the cervix. Of this number, 26 cases of carcinoma of the cervical stump were seen and treated.

2. Most gynecological surgeons consider two years as the dividing line in separating the "true stump cancer" cases from those in which the cancer was present but not recognized at the time of hysterectomy.

3. To the radiologist it is of academic interest whether the case is a true stump cancer or a missed uterine-cervix cancer. Each case requires treatment.

4. In our present surgical era of antibiotics and blood bank, figures quoted by skilled surgeons indicate that mortality following complete hysterectomy is no greater than that seen with supracervical hysterectomy.

5. Our incidence of 10.8 per cent of stump cancer as compared to all cancer of the cervix is higher than that quoted by most writers. If we quote our figure of "true stump cancer" which is 5.4 per cent, it compares favorably with others who have reported.

6. Our five-year survival of 23 per cent is slightly lower than the five-year survival of 26.3 per cent for all cancer of the cervix as reported by nine large clinics.

7. Treatment consists of local treatment to the cervix with radiation, supplemented by external radiation. Most cases in the past have been treated with radium applied locally in the form of a contact capsule or interstitial needles. In our hands, transvaginal radiation has seemed more safe and efficient than locally applied radium.

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Pheochromocytoma (Diagnosis and Use of Regitine During Surgery)

T. K. Lin, M.D.,* and E. G. Dimond, M.D.*

Kansas City, Kansas

The purpose of this paper is to describe the clinical course of a patient with a pheochromocytoma and the use of Regitine®** as a diagnostic and therapeutic agent.

I. Historical Reviews:

In 1886, Frankel[1] reported an autopsy finding of bilateral adrenal tumors and cardiac hypertrophy in a girl of 18 years who had had attacks of palpitation, headache, and vomiting for three years. In 1922, Labbe, Tinel, and Doumer[2] noted the paroxysmal hypertension. The first correct antemortem diagnosis was made by Vaquez and Donzelot[3] in 1926. The following year Mayo[4] performed the first successful removal of a retroperitoneal tumor with paroxysmal hypertension. In 1929, the first case was correctly diagnosed and cured by operation by Pincoff and Shipley.[5] Beer, King, and Prinzmetal,[6] in 1937, demonstrated an increased amount of circulating adrenalin in patients with pheochromocytoma. In 1950, Smithwick[7] gave an excellent clinical differentiation between essential hypertension and pheochromocytoma.

II. General Discussion Regarding the Diagnosis:

The clinical picture produced by pheochromocytoma has been well described repeatedly in medical literature.[7, 47] The correct diagnosis and determination of the exact location of the tumor still presents considerable difficulty because of the protean clinical manifestations, extra-adrenal location, equivocal pharmacological diagnostic tests, and absence of demonstrable adrenal mass. The clinical picture, x-ray findings, and pharmacological tests are essential keys for diagnosis.

However, the demonstration of a pressor substance in blood or urine, when such tests are uniformly used, will probably become the most satisfactory method of establishing the diagnosis.

1. Clinical picture: Clinical history of paroxysmal hypertension, headache, excessive sweating, vasomotor phenomena, elevated temperature, high basal metabolic rate, and glycosuria are typical of adrenal tumors. Persistent hypertension occurs in 25 to 75 per cent of the cases. The absence of headache does not rule out the diagnosis. After removal of tumor, the basal metabolic rate and glycosuria usually return to normal.

2. Roentgenological examination: The flat abdominal film and intravenous pyelograms are of help in larger sized tumors. The finding of adrenal calcification may be of value at times. Perirenal insufflation of air and laminograms may find some small tumors which may be missed by abdominal film and intravenous pyelograms. The occurrence of sudden death following perirenal insufflation has been reported;[7] therefore, the procedure should be done with caution.

3. Pharmacological tests:[48, 56] The following table will demonstrate the number of false positive and false negative tests that have been reported in cases proved by surgery or autopsy.

Adrenal Tumor Testing Agent	*No. False Positive*	*No. False Negative*	*Toxicity or Remark*
Benzodioxane	3	9	Occasional severe hypertensive response.
Dibenamine	7	-	Phlebothrombosis, nausea, psychosis, convulsion, excessive drowsiness and dizziness.
Regitine	8*	1	Least side effect with occasional tachycardia.
Histamine	several	8	Severe headache, induction of paroxysm.
Tetraethyl ammonium cl.	2	3	Tachycardia, sitting position reduces paroxysm.
Mecholyl	-	1	Cardiac arrhythmia marked hypotension, anginal pain; few deaths reported.

* Some patients were uremic.

A battery of pharmacological tests should be carried out in a doubtful case. At the present time, the Regitine® test seems most reliable. In our experience, the mecholyl test has been associated with dangerous reactions such as cardiac arrhythmia, hypotension, and anginal pain.

4. Increased urinary excretion of pressor substances: Various methods of determination of pressor substances have been reported.[57, 64] However, von Euler's method has been more widely applied in pheochromocytoma. Von Euler and Engel[65, 67] have demonstrated definite increase in urinary excretion of norepinephrine and epinephrine in 13 cases of pheochromocytoma. The norepinephrine content has been found to be 50 times greater than normal. An

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** Regitine: Ciba Pharmaceutical Company.

increased ratio of norepinephrine and epinephrine in the urine favors the extra-adrenal location of the tumor. Normal adrenals produced 10 to 30 per cent of the total amount of norepinephrine. In the first six cases of pheochromocytoma (by von Euler), three were located outside the adrenals, all of which contained excessive amount of norepinephrine. It would seem justifiable to explore the doubtful cases with evidence of increased urinary pressor substances. Unfortunately, most of the hospitals are not equipped to run this test.

CASE REPORT

A 54-year-old lady taxi-driver was admitted on December 21, 1951, to the University of Kansas Medical Center complaining of repeated episodes of throbbing headache, pounding heart, blanched face, followed by fatigue and nausea. The patient's description of her attacks, in her own words, was as follows: "The first attack came in September, 1950. It occurred in the evening after dinner. I stooped down to pick up a piece of paper and started feeling sick. I lay down upon the divan and immediately had the feeling that all the blood in my body was rushing to my head. My heart was beating real heavy, and then it all started back down and I felt I was getting better once more. In a few minutes the next attack came, and each time my head hurt worse, but just when I would think I couldn't stand it another moment it would start going back down. I had six attacks over about a three-hour period. In the meantime my husband had called the doctor, but by the time he arrived I was feeling better but very nervous and weak. He took my temperature, blood pressure, pulse, etc., but found nothing seriously wrong.

"These attacks continued over the next 14 months, never as bad as the first one. During a spell, I sweated profusely and afterwards was exhausted and very nervous. The first week of December, 1951, very suddenly I couldn't exert myself at all without bringing on an attack, and I could never connect the episode with anything except perhaps they seemed likely to occur if I was very tired."

Physical Examination: On admission: blood pressure 140/90, pulse 64, respiration 20, temperature 98.6° F. Well developed and well nourished white female, slightly nervous and apprehensive. Fundoscopy: grade ii arteriolar spasm and A-V nicking. Chest and heart were negative. No definite mass could be palpated in the abdomen.

Laboratory findings: Urinalysis: reaction acid, sp. gr. 1.022, albumin trace, few waxy granular casts, 5-6 pus cell, 0-2 RBC/HPF. Blood Count: RBC 4.3 million, Hb. 76 per cent, 11.8 gm., WBC 9800, polys 75, lymph 18, eosinophile 1, monocyte 6. Serology, negative. NPN 37 mgm. per cent, creatinine 1.6 mgm. per cent, sugar 78 mg. per cent, sodium 138 meq. per liter, potassium 4.8 meq. per liter, carbon dioxide 25 meq. per liter, chloride 95 meq. per liter, urea clearance normal, concentration and dilution test normal, PSP 15 min. 26 per cent, 2 hours total 68 per cent.

X-ray findings: Normal heart and lungs. Intravenous pyelogram revealed the right kidney was depressed downward and rotated on its vertical axis. There was a mass (Figure 1) measuring 8 cm. in

Figure 1

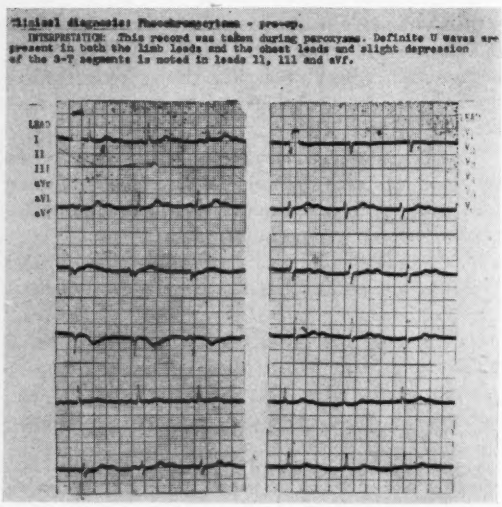

Figure 2

diameter situated in the right adrenal region. Kidney architecture was normal. Normal gallbladder visualization proved the mass on the right was not the gallbladder.

E. K. G. (Figure 2): Sinus bradycardia with a rate of about 60 per minute. Slight depression of the S-T segments in lead II, III and aVf. Marked U waves present in limb and chest leads.

Diagnostic tests: The results of the Benzodioxane®* and Regitine® tests are illustrated in Table 1.

Clinical Course: The patient suffered several paroxysms during hospitalization. The provocative tests with histamine and mecholyl were not considered necessary to substantiate the diagnosis. An abdominal exploration was performed on December 29, 1951, and a cystic mass in the right supra-renal area measuring 10x12x12 cm. was found. The tumor was highly vascular and contained many interwoven dilated veins. Normal adrenal substance was identified at the superior pole of the mass. During the manipulation of the tumor mass, the blood pressure rose from 150/100 to 210/120; however, the paroxysm was well controlled by 11 mgs. of intravenous Regitine® (as shown in Table 1). The tumor weighed 100 gm. after the cystic content was partially lost. The postoperative blood pressure varied from 150/100 to 120/80 on the next day. Cold pressor, histamine, and mecholyl tests were all negative on January 8, 1952 (Table 1). She was discharged on January 9, 1952, with a blood pressure of 120/80. Six months after operation, the patient was completely asymptomatic and her blood pressure was 125/80. The E.K.G. (Figure 3) had returned to normal. She has returned to her job as a taxi-cab driver. The histopathology revealed a be-

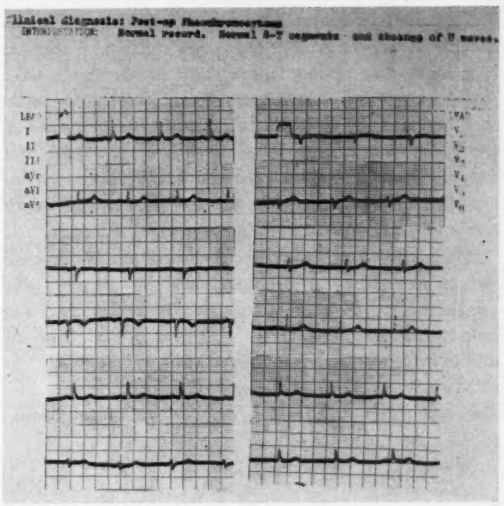

Figure 3

* Benzodioxane: Merck and Company, Inc.

DIAGNOSTIC PHARMACOLOGICAL TESTS

Hosp. Course	Preoperative		During Surgery	Postoperative		
Diagnostic Test	Benadaine I.V.	Regitine I.M.	Regitine I.V.	Cold Pressor	Histamine	Mecholyl
Dosage	20 mgm.	2 mgm.	8 mg. 3 mgm.	ice water (1 min.)	0.025 mgm. I.V.	10 mgm. sub. cut.
B.P	240 220 200 180 160 140 120 100 80 60					
Pulse Rate	140 120 100 80 60 40 20	0 30 60 90 120 150	0 10 20 60 90	35 0 5 10 15 20 25 30 35 50 60	1 2 3 4 5 6 7 8	1 2 3 4 5 10 20 30 40 50 60
Systemic response to diagnostic agent.	Headache, nervousness relieved.	Headache, nervousness relieved.		No symptoms	Mild headache, flushed face	Flushed, perspiring, substernal constriction, dyspnea, apprehension, sl. tachycardia.

TABLE 1

nign type of pheochromocytoma (Figures 4 and 5).

III. Discussion:

Two pharmacological tests (Benzodioxane® and Regitine®) were done on this patient during paroxysms with prompt subsidence of symptoms. The response to the two drugs was identical. No provocative tests were considered necessary.

During surgery, a member of the cardiovascular team was given the responsibility of directing all therapy. A continuous I.V. drip was maintained, and the blood pressure recorded every minute. Spikes in blood pressure upon manipulation of the mass were easily controlled by Regitine®. It was anticipated that the pressure might fall sharply after removal of the gland and Norepinephrine®* was on hand, but no change in pressure occurred. The response to intravenous Regitine® was prompt and easily controlled by regulation of the dose.

Comparison of the electrocardiograms obtained before and after the removal reveals a complete disappearance of the very prominent U waves. Increase in amplitude of the U wave following injection of epinephrine has been reported.[47]

IV. Conclusion and Summary:

1. A description of the paroxysmal episodes experienced by a patient with pheochromocytoma is presented in the patient's own words.

2. The use of Regitine® as a diagnostic and therapeutic aid is described. The use of the drug during surgery aided materially in controlling the dangerous peaks in blood pressure.

3. Prominent U waves, present in the electrocardiogram, disappeared following removal of the tumor. The prominence of the wave may have been due to epinephrine.

* Norepinephrine: Ciba Pharmaceutical Company.

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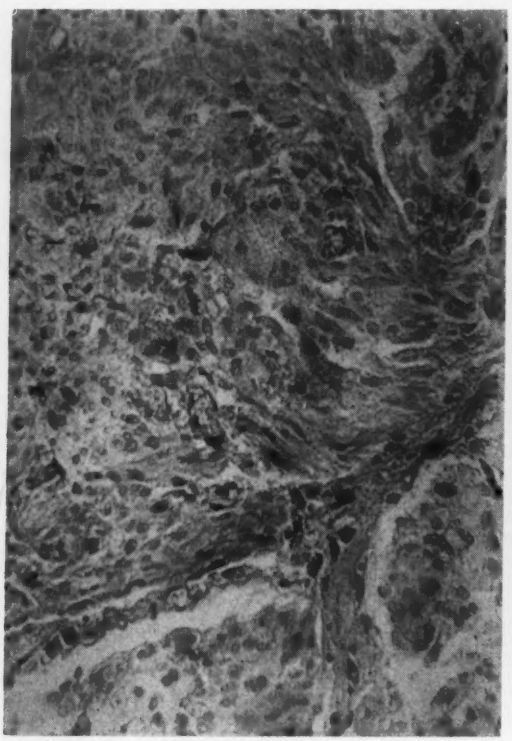

Figure 4

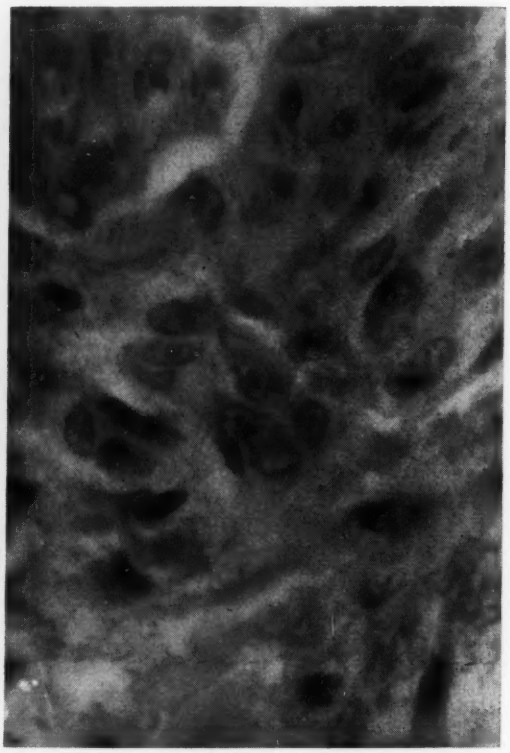

Figure 5

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Two Cases of Chylous Ascites and Chylothorax in Infants with Recovery

Mary J. Blood, M.D.,* and Robert C. Fairchild, M.D.*

Kansas City, Kansas

Idiopathic chylous ascites and chylothorax in infants are relatively uncommon, and the prognosis in such cases is generally considered to be poor. For these reasons we are presenting two cases, in both of which the patients recovered completely in spite of considerable difficulty encountered during the course of their illnesses. The first was a white, male infant, 12½ months of age, who had both chylous ascites and chylothorax intermittently from the age of 9 months until 16 months. The second was a white female infant 4 weeks of age who had chylothorax only.

Case No. 1. K. S., a white, male infant 12½ months old, was first admitted to the University of Kansas Medical Center July 19, 1950, because of recurrent swelling of the abdomen for the previous three months. The referring doctor first noted abdominal enlargement in April, 1950, when the boy was 9 months old, and made a diagnosis of ascites. There was no peripheral or facial edema, and laboratory studies of blood and urine were normal. The ascites disappeared and the patient remained well until June 23, 1950, when he was admitted to a local hospital because of ascites and right pleural effusion. A mercurial diuretic was given, and the pleural fluid and most of the ascites receded within a few days. He remained well until July 17, 1950, when the ascites recurred and the patient was referred to the University of Kansas Medical Center.

Past history was non-contributory. The birth was normal. Developmental and family history were not relevant.

Physical examination on admission revealed a well-developed and fairly well nourished white male who was not acutely ill. Weight was 26½ pounds. Height was 31½ inches. The face and extremities were thin. The abdomen was protuberant, and a fluid wave could be elicited. Genitalia were normal without edema. There was no lymphadenopathy. The legs were slightly "bowed." Examination was otherwise not unusual.

Laboratory procedures: Histoplasmin and tuberculin skin tests were negative; serology was negative; stool examination showed no blood, ova or parasites. All urinalyses were normal. Blood counts revealed slight secondary anemia, 3,400 Wbc's with 68 per cent polymorphonuclears, 27 per cent lymphocytes and 5 per cent mononuclears. The white count remained below 6,250, and the differential remained essentially the same as on admission except for an occasional eosinophile. His blood showed an NPN of 37.5 mg. per cent, CO_2 combining power of 25 meq./1, serum calcium of 10.2 mg. per cent. Liver function tests were all within normal limits. A fat determination on a 24-hour stool was normal. The fat and protein concentrations of blood and chylous fluid are given in Tables 1 and 2.

TABLE 2.

STUDIES OF CHYLOUS FLUID REMOVED FROM PATIENT K.S.

Date	*Color*	*Sp. Gravity*	*Protein*	*Fat*
7/21/50	White	1.013	2.1 Gm%.	5.76 Gm%.
7/27/50	White	1.010	1.03	6.75
8/9/50	White	1.009	0.68	5.73
9/11/50	.....	.....	3.9	.....

X-ray of the chest on admission was normal. On August 2, 1950, fluid was demonstrated roentgenographically in the right pleural cavity, displacing the heart to the left. Intravenous pyelograms and upper gastrointestinal series were interpreted as normal. X-ray examination of the long bones showed some anterior bowing in the lower extremity, but was otherwise normal.

Hospital course: Abdominal paracentesis was performed two days after admission, and 150 cc. of

TABLE 1.

BLOOD PROTEIN AND LIPID VALUES OF PATIENT K.S.

Date	*Cholesterol*	*Chol. Esters*	*Total Protein*	*Alb.*	*Glob.*	*Total Lipid*
7/20/50	.....	.....	6.8 Gm%.	4.85	1.95	.....
7/26/50	205 mg%.	85%	6.5	4.66	1.84	820 mg%.
8/8/50	.....	.....	5.7	4.02	1.68	980
8/21/50	243	69%	.....	....	....	.....
10/26/51	222	.....	.....	....	....	660

* Department of Pediatrics, University of Kansas Medical Center.

milky fluid was obtained. Six days later, 125 cc. of fluid was removed. The boy was somewhat irritable but was otherwise well except for the ascites. Following the initial paracentesis, the patient was placed on a low fat, high protein diet. On August 1, 1950, 25 mg. of Sudan III in 5 grams of butter was fed to the patient, and paracentesis 6 hours later revealed pink-tinged ascitic fluid which was, however, microscopically negative for Sudan III.

The patient had an increase in respiratory rate, dullness in the right lower chest and dsypnea during the next two days, necessitating thoracentesis on August 3, 1950. The pleural fluid was pink in color and identical to the chyle obtained by paracentesis. The color was thought to be due to the Sudan III. A total of 1000 cc. of chyle was removed from the chest on August 8 and August 31 in order to relieve dyspnea. During this time the circumference of the abdomen varied from 51 to 57 cm. The administration of mercurial diuretics did not diminish the ascites.

On August 14, 1950, Dr. Thomas G. Orr, Sr., performed Routte's operation, a venous-peritoneal anastomosis of the left saphenous vein. The abdomen was drained at surgery, but exploration was not done. The postoperative course was satisfactory. There was beginning abdominal distention on August 17, 1950, and a definite fluid wave was felt on August 22, 1950. The chest remained clear and, because the abdomen had ceased to increase in size, the patient was discharged on August 26, 1950, his 9th postoperative day. On discharge the abdomen measured 48 cm. in circumference; a fluid wave was palpable. The chest was clear, and the patient appeared well except for the ascites. He was discharged on a low fat, high protein diet with vitamin supplements. During hospitalization he had received antibiotics only for several days following each paracentesis and postoperatively.

On September 2, 1950, one week after discharge, the patient was readmitted with acute respiratory distress. On the day prior to admission, the boy had received a penicillin injection for acute tonsillitis. On the day of admission a right pleural effusion was noted. Examination showed a dyspneic white male 14 months of age who was acutely ill and cyanotic when lying supine. Respirations were rapid and shallow. Bilateral otitis media, pharyngitis, and pleural effusion on the right were present. The right chest was flat from the midscapular area to the base, and breath sounds were absent in this area. Hyperresonance of the left chest prevented accurate percussion of the heart. The abdomen contained fluid and measured 47.5 cm. in circumference.

A right thoracentesis was done immediately, and 600 cc. of the same type of fluid as on previous occasions was removed. The respirations improved, cyanosis disappeared, and the patient obtained considerable relief from the procedure. He was placed on chloromycetin and penicillin with clearing of the otitis media and pneumonia of the right base (confirmed by x-ray) by September 6, 1950. His abdomen increased in circumference to 61 cm. during the next few days, and on September 11 both paracentesis and thoracentesis were performed. Thoracenteses were repeated September 19 and September 28, the total amount of fluid removed being approximately 1000 cc. On September 28 the circumference of the abdomen was 54 cm.

A right saphenous-peritoneal anastomosis was performed September 29. Following surgery the circumference of the abdomen was 51 cm. Six days later it measured 57 cm., and a right pleural effusion was again demonstrated. Thoracenteses were done on September 5 and October 10 and a total of 475 cc. of chylous fluid was removed.

Study of the clinical course revealed that whenever there was a gradual increase in abdominal distention, this was followed by roentgenological evidence of a shift of the heart and mediastinum to the left and the appearance of a left upper mediastinal shadow, and in the next day or so a pleural effusion on the right. This cycle was noted twice and seemed to take about nine days for completion. All chest x-rays showed marked elevation of the diaphragm on the right.

The right pleural effusion cleared by October 24, 1950. Although there was some ascites present, it was not marked and there was no further abdominal distention. The patient appeared in good health except for the slight ascites, and was discharged on November 11, 1950. During this second hospitalization red cell count and hemoglobin were normal. The white count varied from four thousand to six thousand with 64 to 72 per cent polymorphonuclears and 0 to 10 per cent eosinophiles. The chylous fluid was the same in character as on his first admission.

Follow-up visits during the past two years revealed the abdominal distention to have disappeared by April 28, 1951, four and one-half months after discharge. He had had several respiratory infections but was well when seen on October 26, 1951. There was no edema of either thigh, and an x-ray examination of the chest was reported as normal. Serum lipids were 660 mg. per cent and blood cholesterol was 222 mg. per cent. On March 10, 1952, the patient weighed 35½ pounds and was a normal appearing 2½-year-old boy. He is still being maintained on a low fat, high protein diet.

Case No. 2. D.J.L., a white female infant four weeks of age, was admitted to the University of Kansas Medical Center on January 15, 1952, five days following the onset of suprasternal and lower costal retraction, dyspnea, coughing, and vomiting,

without fever or cyanosis. The patient had been placed on aspirin, orange juice and a red liquid medication with some improvement. On the day of admission fluoroscopy revealed air and fluid in the right chest. Past history was not unusual and family history was non-contributory.

Examination on admission revealed a well-developed, well-nourished infant with moderate respiratory distress, slight suprasternal and lower costal retraction, and shallow respirations with a lag of the right chest. Percussion revealed dullness in the right chest posteriorly to the level of the eighth rib. Breath sounds and vocal fremitus were decreased in the right base posteriorly, and fine rales were heard in the right chest anteriorly. The left lung was clear.

The liver was enlarged to the iliac crest; the abdomen was otherwise not unusual. A hemangioma 1.0 cm. in diameter was in the skin near the left nipple. The rest of the examination was not unusual. Temperature on admission was 98.0° F.

Urinalysis on admission was normal. Complete blood count showed 3,500,000 Rbc's, 10.9 Gm. Hgb., 6600 Wbc's, 42 per cent polymorphonuclears, 51 per cent lymphocytes, 6 per cent monocytes and 1 per cent metamyelocytes. Chest x-ray on admission revealed right hydrothorax and a widened mediastinum.

On the day following admission, a right thoracentesis was performed and 50 cc. of white milky fluid was withdrawn. This provided considerable relief of the patient's dyspnea. She was placed on penicillin, terramycin, and a skim milk mixture fortified with dried skim milk. The fluid withdrawn from the chest was milky, separated into a creamy layer on standing, contained 1.4 gm. per cent of fat, 3.8 gm. per cent of protein, was sterile and contained no malignant cells on pathological examination. Blood studies were done for cholesterol, total lipids and total proteins (Table 3). The patient's clinical improvement continued for one week, whereupon she was given milk containing 3.8 gm. carbohydrate, 0.99 gm. protein and 0.36 gm. fat per ounce. Two days later she was again dyspneic, and an x-ray examination revealed considerable fluid in the right chest. Thoracentesis was repeated on that day, the following day and three days later because of persistent dyspnea, a total of 340 cc. of chylous fluid being removed (Table 4). She was put back on the skim milk mixture and was dismissed two days later, her 16th hospital day, apparently symptom-free. Two days following discharge from the hospital the patient was again dyspneic, and thoracentesis yielded 200 cc. of cloudy yellow fluid which was sterile. Follow-up examination one month after discharge revealed a weight gain of 2 pounds, clear lung fields by x-ray, normal sized liver, and normal physical findings. She is still well 11 months after discharge.

TABLE 4.

THORACENTESES PERFORMED ON PATIENT D.J.L. AND STUDIES OF THORACENTESES FLUID

Date	*Amount*	*Color*	*Protein*	*Fat*
1/16/52	50 cc.	Milky-white	3.8 Gm%.	1.4 Gm%.
1/25/52	60 cc.	Greyish-white	4.3	462 mg%.
1/26/52	100 cc.	Greyish-white	3.6	366 mg%.
1/29/52	180 cc.	Milky-white	3.0	.....
2/2/52	200 cc.	Cloudy yellow	....	.....

DISCUSSION

Milky effusions have been classified as chylous, chyliform and pseudochylous. Blankenhorn proved by experiments that no criteria exist whereby chylous fluids can be distinguished from other milky fluids and that the milkiness is due to finely-divided fat in all cases.[1] We believe that the terms "chyliform" and "pseudochylous" should be discarded and all milky fluids should be designated simply as "chylous."[1, 2, 3]

Our first case, together with those found in the literature, makes a total of 50 cases of chylous ascites in children 15 years of age or younger.[4, 5, 6, 7] Twenty-five of these cases occurred in the age group from birth to two years. Our second case makes a total of 28 cases of chylothorax in children 15 years of age or less. Eighteen of these occurred in infants.[2, 3, 4, 8, 9]

The etiology of chylous ascites in children has been varied, including abdominal tumors, tuberculous peritonitis or adenitis, acute heart disease, and a few cases of abnormality of the thoracic duct. However, the largest number are idiopathic in origin and represent 17 of the 50 cases. In the age group from birth to two years, there are 14 cases of idiopathic chylous ascites. The cases of chylothorax in children include 11 of unknown origin, all in children two years of age or less. Thus, in both chylous ascites and chylothorax, the etiological agent is most frequently unknown, and this occurs more often in infants than in older children.

TABLE 3.

BLOOD PROTEIN AND LIPID VALUES OF PATIENT D.J.L.

Date	*Cholesterol*	*Total Protein*	*Alb.*	*Glob.*	*Total Lipid*
1/10/52	64 mg%.	5.40 Gm.%.	4.53	0.87	421 mg.%.
1/23/52	162	.....	.....	.....	744
1/30/52	148	5.55	4.45	1.10	625

The mortality from both chylous ascites and chylothorax in children is about 33 per cent. Of the 50 cases of chylous ascites, there were 16 deaths. There were 9 deaths in the 26 cases of chylothorax in which the outcome is known. In children under two years of age, 6 with chylous ascites and 7 with chylothorax died. Of the infants dying with chylous ascites, only one was classified as idiopathic. Four of the cases of chylothorax in infants who expired were of unknown origin. No relationship between etiology and mortality can be established.

Death in idiopathic cases is thought to be due to cachexia from frequent withdrawal of the chyle and the resultant loss of protein, fat, electrolytes and fluid. Bauersfeld indicates that death will ensue in three weeks if leakage of chyle is great and withdrawal is frequent.[10]

Therapy in cases of chylous ascites and chylothorax is usually conservative, thoracic or abdominal paracenteses being performed only to relieve pressure symptoms. The chyle removed during the procedure has been returned to the patient by intravenous infusions in some cases. Two deaths have been reported from this procedure. Forbes felt that his patient, an infant 6 weeks of age who received 14 infusions of chyle without reaction, was possibly benefited by this treatment. A low-fat high-protein diet is recommended as a means of reducing the volume of chyle produced. Since the fat-soluble vitamins are largely lost in the chylous fluid, the administration of water-miscible vitamin preparations is deemed advisable.

Attempts to explore the thoracic duct are usually inadvisable. Postmortem examinations often show no abnormality of the duct or its terminals, and in some cases the thoracic duct is not even found. Ligation of the thoracic duct in adults has been recommended by Schaffner and Kirkpatrick.[11] Since exploration for the thoracic duct is especially difficult in children, operations to drain chyle from the peritoneal cavity by a new route have been devised for relief of chylous ascites.[12, 13] The Routte operation is based upon use of the saphenous vein to produce a venous-peritoneal anastomosis. In cases of chylothorax, permanent suction drainage to allow formation of adhesions in an effort to close the defect in the duct has been tried.

It is of interest to note that in both of our cases widening of the mediastinal shadow on x-ray was observed either preceding or coincident with the appearance of right hydrothorax. This may be partially explained by the anatomy of the thoracic duct.[14] Griffith postulates that traumatic tears in the thoracic duct would be expected to lead to accumulation of chylous fluid near the tear. He states that tears in the duct in the lower thorax are more likely to result in right-sided chylothorax, while tears in the upper thorax more likely lead to a left-sided effusion.[15] In either case the leakage of chyle would first be into the mediastinum with subsequent rupture or filtration into the pleural cavity.

It seems logical to assume that the same mechanism could occur in spontaneous chylothorax, and this appears to be borne out by the x-ray findings in these two cases. The possibility exists that chylous fluid from the peritoneal cavity could leak into the mediastinum and thence into the pleural cavity or vice versa. The occurrence of chylous ascites and right chylothorax from high thoracic duct obstruction has been reported,[16] but was believed to be due to rupture of the distal lymphatics from increased pressure. There is no constant relationship between chylothorax and chylous ascites and one may develop with or without the other.

SUMMARY

Two cases of chylous effusions in children are presented, both resulting in apparent recovery. The frequency, etiology, mortality, prognosis, and treatment of chylothorax and chylous ascites are discussed, together with speculation on some of the unusual aspects of these two cases.

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Atresia of the Tricuspid Valve with Large Interauricular Septal Defect, Pulmonary Stenosis and Patent Ductus Arteriosus

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This is an infrequent congenital malformation of the heart. With recent advances in cardiac surgery, accurate clinical recognition becomes ever more imperative. The following case is reported because it illustrates that the electrocardiogram alone may be sufficiently characteristic to enable the diagnosis to be made during life. It is hoped that this report will help others to recognize this unusual congenital heart disease.

REPORT OF A CASE

M. G., a male child, born at St. Mary's Hospital, was cyanotic at birth and had moderate respiratory difficulties. He was kept in oxygen for the entire first week of life. There was a rather harsh systolic murmur best heard along the left sternal border. No thrills could be felt. Laboratory findings, including blood count, urinalysis and Wassermann test, were within normal limits. Chest x-ray was interpreted as dextrocardia (Figure 1). An electrocardiogram taken on the second day after birth, including leads over the right and left thorax (Figure 2), showed marked left axis deviation, regular sinus tachycardia with the PR and QRS intervals within normal limits. The transitional zone was shifted to the right, and there was evidence of left ventricular hypertrophy. In view of these findings the electrocardiographic diagnosis was: congenital heart disease, atresia of the tricuspid valve with possible interauricular septal defect.

About two weeks after birth the infant's color improved and he was allowed to go home.

At the age of about eight weeks, he suddenly became very cyanotic and was rushed to the University of Kansas Hospital where he died 45 minutes after admission. Autopsy performed by Dr. Moriarty showed the following positive findings:

"On opening the chest nothing unusual was seen except that the heart lay in a rather transverse position and the left ventricle lay slightly to the right of the midline. It was found that the heart had one very large ventricle, which was the left, and the right ventricle was quite small, the pulmonary vessels coming off the right ventricle also being quite small. There was atresia of the tricuspid valve. The mitral valve was not unusual. The pulmonary valve measured but 1 cm. in circumference. The ductus arteriosus was patent. There was a large interauricular septal defect. The capacity of the right ventricle was not more than 5 cc. at the very greatest. The liver extended about two fingers breadth below the costal margin on the right. Anatomical diagnosis: congenital heart disease, tricuspid hypoplasia with large interauricular septal defect, patent ductus arteriosus and pulmonary stenosis."

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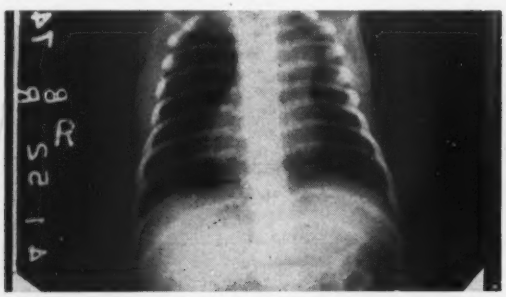

Figure 1. The cardiac shadow is of such configuration as to suggest dextrocardia. There is rather smooth prominence in the left superior mediastinum which shows marked pulsation. Transmitted pulsation from an enlarged thymus cannot be excluded. Abdominal viscera show normal position.

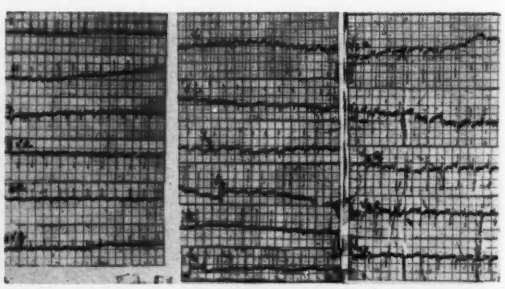

Figure 2. Taken first day after birth. The electrical axis is approximately plus 25° (normal for infants 120° or more). There is regular sinus tachycardia. The transitional zone is in V3r (right thorax). Only V6r and V7r show right ventricular pattern. All other chest leads show transitional or left ventricular pattern. These findings are typical of atresia of the tricuspid valve with diminutive right ventricle.

COMMENT

The essential feature of the malformation in this case is the diminutive right ventricle. This is always associated either with tricuspid atresia or hypoplasia and a severe malformation of the pulmonary tract. If there is pulmonary atresia, there must be a patent ductus arteriosus in order to have circulation compatible with life. If the right ventricle does not function, the blood is unable to leave the right auricle; some patency in the interauricular septum is therefore inevitable.

Though the malformation under discussion is a right sided lesion, the electrocardiogram shows a left axis deviation. It is the only malformation of the cyanotic group associated with such marked electrocardiographic changes. In the infant under six months of age, the electrical axis of the heart is normally greatly to the right. This physiological deviation is even more pronounced in almost all congenital cardiovascular defects like pulmonary stenosis, the tetralogy of Fallot, and interauricular septal defect. It becomes important, then, to realize that the electrocardiogram is an excellent aid in the diagnosis of the malformation under discussion. In fact in our case it was the only test that permitted a correct diagnosis ante mortem. Cases of tricuspid atresia with non-functioning right ventricle and auricular septal defect, as well as those of non-functioning right ventricle with auricular septal defect, pulmonary atresia and patent ductus are now amenable to surgery.

SUMMARY

1. A case of tricuspid atresia with pulmonary stenosis, large interauricular septal defect and patent ductus arteriosus is reported.

2. The importance of the electrocardiogram in making a correct ante mortem diagnosis is stressed. The malformation under discussion is the only one of the cyanotic group to be associated with left axis deviation.

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Radiographic Diagnosis of Placenta Previa

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The incidence of placenta previa varies in most reports from one in 100 to one in 300 obstetrical cases. Its presence constitutes a serious complication of pregnancy, but one which can be successfully handled if recognized. The appearance of painless bleeding in the third trimester is usually due either to placenta previa or to premature separation of a normally implanted placenta. The differentiation between these two possibilities is markedly facilitated by identifying the site of the placenta radiographically.

The radiographic method we are employing to demonstrate the placental site is based on soft tissue technique originally described by Snow[1] and later modified by Ball and Golden[2] and Reid.[3] Three projections are made without contrast media, and they can be used as routine views on all patients studied by x-ray in the last trimester for other indications as well as in those suspected of having a low placenta implantation. The method has the advantage of requiring no unusual equipment and of giving information, if needed, regarding the maternal pelvis with measurements, fetal head measurement, and information regarding the condition of the fetus. All projections are made upright, using a Bucky diaphragm and a 40 inch-anode-film distance. The distance may be changed as long as it is accurately measured and recorded. The bladder is emptied just before the films are made.

The three projections are as follows:

1. A.P. upright, 40 inches, 14 by 17 film, 200 M.A., 1 sec., K.V. according to patient's thickness. This projection must include the pubis, ischial tuberosities and both greater trochanters, as well as the major portion of the abdomen.

2. Lateral pelvis, upright, 40 inches, 10 by 12 film, left side nearest the film, 200 M.A., 1¾ sec., K.V. according to patient's thickness. The film must include the sacral promontory, symphysis pubis, sacrum and coccyx, ischial tuberosities, and the fetal head. These bony landmarks are necessary in order to make pelvic measurements if indicated.[4]

3. Lateral fetus upright, 40 inches, 14 by 17 film, left side nearest the film, 200 M.A., 1 sec., K.V. according to patient's thickness. This film is to include the entire uterine wall as low as the symphysis

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pubis. We have employed a crescent-shaped wedged filter in this view on very heavy patients to show the anterior wall in greater detail without under penetration of the bony landmarks, but it is not essential.

The placenta is a saucer shaped organ having the density of fluid, usually measuring 3 to 4 cm. in thickness in the radiographs. It is more dense than the fatty tissue located in the subcutaneous fetal structures, and is of greater thickness than the uterine wall, which usually measures 1 to 1½ cm. The diameter of the placenta varies considerably, covering a distance of approximately 15 to 20 cm. in a patient near term. Since the average size of a pregnant uterus near or at term is approximately 30 to 35 cm. from the upper to lower pole, placenta previa marginalis is probably present if the bulk of the placenta is visualized below the equator of the uterus.[5]

A normally implanted placenta can be visualized in the fundus on the lateral upright film in a majority of cases. Its identification is relatively easy if it is implanted directly anterior, posterior or superior to the fetus. An additional aid in recognizing the soft tissue structures of the placenta is the presence of physiologic calcification which occurs in approximately one-third of the cases.[6] If the implantation is oblique, either partially or wholly on a lateral wall, both A.P. and lateral projections are studied. The A.P. film shows a soft tissue shadow, usually poorly defined, between the fetal parts and fat line, and the intestinal gas of the maternal abdomen.

The identification of the normally implanted placenta assumes a greater accuracy as one's experience in viewing the films increases. Needless to say, it is highly dependent on the technical excellence of the films. If the films are improperly made due to poor positioning, over or under penetration, motion of the patient, or dark room errors, an interpretation of the placental site should not be attempted.

When the placenta is definitely established to be present in the fundus of the uterus, with its bulk above the equator, one can unequivocally state, "No placenta previa is present." For this reason we believe that the first step in radiographic study for placenta previa should be the determination of its presence or absence in the fundus. If it is not identified in the fundus on adequate projections, a low implantation is highly probable, and the three films are then examined for evidence of displacement of fetal parts from their usual position. This is most readily determined in the case of vertex presentations, which occur in about 95 per cent of all cases,

Figure 1. Lateral fetus projection showing placenta on superior and posterior wall of uterine fundus.

Figure 2. A.P. upright view showing fetal head displaced from the midline by a low placental implantation.

breech and transverse presentations accounting for about 4.0 per cent and 1.0 per cent respectively.

It was first emphasized by Ball and Golden in 1943 that in the last trimester a normal cephalic presentation dips into the pelvic inlet and occupies a mid-coronal and mid-sagittal plane position if the mother is upright. If the patient is horizontal, the head shifts in relation to the inlet with a change in her position due to the pull of gravity on the fetal head.[7] Therefore, it is necessary to place the patient upright in these projections if one is to evaluate the soft tissues for evidence of a low placenta. Of course the bladder should be empty, as a full bladder will displace the head upward and prevent its entering the pelvic inlet. Disproportion between the size of the fetal head and pelvic inlet will also prevent its entering the pelvis, but this can be ascertained by measurements of fetal head circumference and pelvic inlet from the A.P. and lateral films.[4]

The midline position of the fetal head in relation to the maternal pelvis in normal placental implantation has been studied in detail by Reid.[8] He found the distance of the presenting part from the sacral promontory and inner margin of the pubic symphysis to be less than 1.5 cm., and he believes this measurement may be used as a standard in a fetus near term in the upright position. Placenta previa marginalis or partialis will increase this distance to 2.5 cm. or more as the head is displaced by the placenta forward or backward. These measurements are easily obtained from the lateral film.

If the placenta is laterally implanted in the lower uterine segment, the head will be shifted to the right or left in the A.P. view. Displacement of the fetal head from the mid-sagittal plane or mid-coronal plane, or both, is strongly suggestive of placenta previa partialis, particularly when the placenta is not identified above in the fundus, or when identified below the mid-line of the uterus. If the head is displaced, but the placenta is visualized above, it may be evidence of a pelvic tumor.

Placenta previa centralis displaces the head directly upward, and in the absence of disproportion or distended bladder, and with the placenta not visualized elsewhere, the diagnosis is probable. Frequently a soft tissue shadow can be seen producing a smooth rounded defect on the anterior wall of the gas-filled rectum as corroborating evidence of central placenta previa. Occasionally there is indefinite visualization of the placenta above in the fundus, and the head is uniformly displaced upward. In such cases fluid in the amniotic sac from unruptured membranes may be confused with central placenta previa, but can be differentiated by palpation on rectal examination.

In a high percentage of cases, placenta previa centralis, partialis, or marginalis can be established or ruled out by the method outlined above. If the findings are inconclusive, the additional procedure of cystography can be carried out, using an aseptic injection of air or Skiodan 10 to 20 per cent into the bladder.[9] The urinary bladder contacts only the anterior wall of the lower uterine segment, and usefulness of the cystographic method is therefore limited to those cases with placental implantation in the anterior area. We have seldom found it necessary to utilize cystographic studies to confirm the presence of low placental implantation as the soft tissue studies are usually conclusive.

CONCLUSIONS

A radiographic method of determining the site of the placenta in normal and low implantations is described.

An accurate study can be obtained in the last trimester using soft tissue technic without the use of contrast media.

The importance of making the projections in the upright position is emphasized as necessary in diagnosis of placenta previa.

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Cyst of the Left Adrenal Gland

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Inasmuch as cysts of the adrenal glands are not common, a report of a recent case is presented.

The patient was a 72-year-old white man who died suddenly. He was not under the care of a physician. The autopsy revealed extensive coronary atheroma with partial occlusion, a heart weighing 470 grams with a flabby musculature, and a tricuspid ring measuring 15 cm. in diameter. Consequently, cardiac collapse was regarded as the cause of death. Nothing else worth noting was present except a unilateral enlargement of the adrenal glands. The right adrenal weighed 12 grams and appeared normal.

The left adrenal was much enlarged, weighing 178 grams and including a cystic mass 6.5 cm. in diameter. The cortical tissue was unusually abundant. The cyst wall was well outlined and largely enclosed by adrenal cortical tissue. The cyst contained 75 cc. of a grummy, granular, opaque, pale yellow, semifluid material. Occasional streaks of blood-tinged material could be seen. Much necrotic cellular debris appeared to be present. The cyst wall was fibrous with small islands of cortical adrenal tissue incorporated. A part of the adrenal cortex was flattened over the cyst wall. Much of the adjacent adrenal cortical tissue was markedly hypertrophied. Multiple sections failed to reveal recognizable medullary tissue.

Microscopic examination showed well marked cortical hypertrophy and some adenomatoid areas. The wall of the cyst was largely fibrous in character with a ragged, roughened inner surface. It contained clumps and clusters of cortical tissue more or less atrophied. In other areas there were masses of necrotic cellular tissue in which clusters of hyperchromatic nuclei could be recognized. Some of these were large and irregular in size and shape. In fact, the cytology and pattern suggested a broken down and degenerated pheochromocytoma with cystic autolysis. This would indicate that the cyst was the result of softening and liquefaction of an adenoma of the medullary tissue.

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Cyst of left adrenal gland

Of the cysts of the adrenal gland reported in the literature, the type following cystic autolysis of an adenoma of either the cortex or medulla, such as in this case, is one of its more common types. Henchen divides cysts of the adrenal glands into three groups, viz:

1. Parasitic cysts e.q. echinococcus (rare).
2. True cysts lined by either epithelium or endothelium. Epithelial lined cysts are rare. Cysts lined by endothelium are more common, often giving rise to lymphangioma or lymphangiectasis.
3. False cysts resulting from a cystic degeneration of a hematoma or of an adenoma. The incidence of this type is high, but it is difficult to determine its relative frequency since a study of reported cases frequently lacks the details to determine the origin of the cysts. For instance, Stock, in 1947, reported 50 cases in the literature, but his account leaves much doubt on the frequency of the cystic adenoma.

The clinical significance of the adrenal cyst is variable. They are more common in women than in men, and in most instances are found on the left side. The smaller cysts are often recognized as abnormal masses between the renal region and the diaphragm and in the posterior part of the abdominal cavity. They may be recognized clinically and have even been successfully removed surgically, such as the cases reported by Doran and Ballance.

Most cases were recognized at autopsy, though the larger forms were often recognized clinically. The cyst reported by Ballance was found on routine inspection while doing a laparotomy for a duodenal ulcer, and it was successfully removed surgically at a later date. Another case was found at autopsy two days after a cholecystectomy. Stock reported a cyst that was palpated and removed in a patient undergoing a Smithwick thoracacolumbar sympathectomy. Another patient presented a multiglandular syndrome believed to be thyroid and parathyroid dysfunction. In still another instance, the patient exhibited shock, acute abdominal pain, and palpable abdominal tumor

that became apparent over a three-day period. Doran's case entered the hospital complaining of abdominal swelling and pain. Adrenal cysts are often large and massive retroperitoneal tumors, such as the case of Zuckner in which the cyst contained 2,000 cc. of clear, yellow fluid.

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The Repair of Large Abdominal Wall Defects with Fiberglas* Fabric**

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Occasionally the surgeon is called upon to repair massive defects of the abdominal wall. Closure without tension often cannot be accomplished without the aid of autogenous tissues, metals or plastics. Foreign inert material should be used only when repair cannot be accomplished by any other method. Autogenous grafts of fascia, cutis[1] or whole skin[2, 3, 4] have been used in reconstruction, but their use is sharply limited by the size of the defect.

Metallic prostheses of silver wire coil[5] or filigree,[6] tantalum[7, 11] and stainless steel mesh[12, 13] have been used with varying degrees of success. Silver wire has been discarded because of fragmentation and its electrolytic effect. Tantalum mesh has had an extensive experimental and clinical use in repairing a wide variety of defects. Favorable reports attest to its tissue tolerance in the reconstruction of hernia,[14, 16] diaphragm,[17] chest,[18] abdominal wall defects,[19] and defects of the skull.[20]

Tantalum is malleable, strong, and more resistant to infection than stainless steel. It has a minimum electrolytic effect. Fibroblastic growth takes place through the interstices of the mesh, adding to the strength of the repaired area. Tantalum mesh, however, does undergo fragmentation when it is used in areas subjected to a constant shearing stress. In spite of this disadvantage, the repaired area remains strong and supple.

Fibroblastic growth does not infiltrate stainless steel mesh. A dense scar envelops the steel mesh forming a thick bursa.

A regenerated inert cellulose acetate yarn (Fortisan††)[21] has been used experimentally and clinically in the repair of abdominal defects. This fabric readily withstands autoclaving. A minimal tissue reaction was reported with less leukocytic infiltration around the implant as compared to an experimental control series of stainless steel mesh.

Fiberglas cloth was utilized by us as a prosthesis in repairing large abdominal wall defects both experimentally and clinically. Fiberglas is inorganic, durable, flexible and does not shrink. The tensile strength is greater than cotton or rayon. The fabric does not absorb moisture and is insoluble to organic solvents. Sterilization can be readily accomplished by autoclaving as the fiber strength begins to decrease only at temperatures of 600° F. In the manufacture of the cloth, a starch water soluble binder is applied to prevent fibers from abraiding in the weaving operation. This binder is innocuous and does not produce any untoward tissue reaction.

EXPERIMENTAL METHOD

Eight mongrel dogs were operated on under intravenous sodium pentothal anesthesia. In three of these animals the right anterior rectus sheath and muscle were removed (5 by 10 cm.). A single layer of Fiberglas was sutured into the defect with 4-0 interrupted black silk. The skin was closed over the Fiberglas

* Fiberglas is the trade-mark of Owens-Corning Fiberglas Corporation, Toledo, Ohio.
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†† Product of the Celanese Corporation of America, 180 Madison Avenue, New York 16, New York.

without drainage. Fiberglas fabric tends to fray somewhat when cut to pattern. Prior to fixation into the defect, the edges of the cloth are folded over for 1 cm. and basted with a running locked sailmaker's stitch. This suture also gives an additional point for fixation to the surrounding tissue. In one animal both anterior recti sheaths and muscles were removed (9 by 9 cm.). The resultant defect was replaced with Fiberglas.

In four animals a full thickness of abdominal wall was removed, including the peritoneum (6 by 8 cm.). The defect was closed with a double layer of Fiberglas cloth. The skin was closed over the fabric.

All of the eight animals survived the operative procedures. They were sacrificed at monthly intervals up to the eighth month in order to observe the effects of tissue tolerance and healing.

RESULTS OF ANIMAL EXPERIMENTS

Clinically there was no evidence of postoperative hernia in any of the animals. The repaired areas were strong and supple. The incisional scar moved freely over the inserted cloth. The Fiberglas was well tolerated and did not spontaneously extrude. Serial sacrifices showed fibroblastic infiltration into the cloth. At the edges of the surgical defect, the surrounding tissue had grown into the fabric. No purulent exudates were present in the sacrificed animals. Minimal adhesions were present between the bowel and the Fiberglas in those animals in which the peritoneum was removed. No bowel obstruction was noticed in the series. Encouraging results from the above animal experiment led to its clinical use.

Case 1. J. F., a white, 55-year-old male, was admitted to the University of Kansas Medical Center on February 13, 1952. The patient had had a bilateral inguinal hernia for 30 years. A bilateral inguinal herniorraphy had been done one year previously. The left testicle and cord had been removed in performing the repair. On February 18, 1952, under spinal anesthesia, a right inguinal hernioplasty was done utilizing a Fiberglas prosthesis for the repair. All of the tissues encountered in dissection were of poor quality. Direct and indirect herniae were present, each measuring 5 cm. in diameter. The direct sac was converted by the Hoguet maneuver, and the neck of the indirect sac was tied by a purse string suture of 3-0 black silk. The excessive redundancy was amputated and the neck transfixed. A frayed conjoined tendon was sutured to the shelving portion of Poupart's ligament, mainly to obliterate space. A double layer of Fiberglas (5 by 20 cm.) was placed beneath the cord. A hiatus for the cord was made superiorly. The cloth was then sutured laterally to Poupart's ligament, inferiorly to the periosteum of the os pubis and medially to the substance of the conjoined tendon, by means of a continuous suture of stainless steel. A relaxing incision was made obliquely in the rectus sheath to allow suture of the external oblique fascia to Poupart's ligament without tension. The cord was then transplanted subcutaneously and the skin closed in the usual fashion. On March 4, 1952, the patient had a repair of the hernia on the left side. The patient was discharged on March 20, 1952.

Comment: This patient has had no evidence of recurrence nine months after operation. Fiberglas provided a ready means of reconstruction in this hernia. The tissues were of such poor quality that their use alone would have jeopardized the repair.

Case 2. I. G., a 60-year-old, colored female was admitted to the University of Kansas Medical Center on July 25, 1952. Five weeks prior to admission, she noticed a mass in the lower abdomen gradually increasing in size (8 by 10 cm.). The mass was firm, tender, inflamed and was situated between the pubis and umbilicus. A urological survey showed the dome of the bladder to be invaded with tumor. On August 5, 1952, under continuous spinal anesthesia, a full thickness of the abdominal wall, including the tumor mass, peritoneum and involved urinary blad-

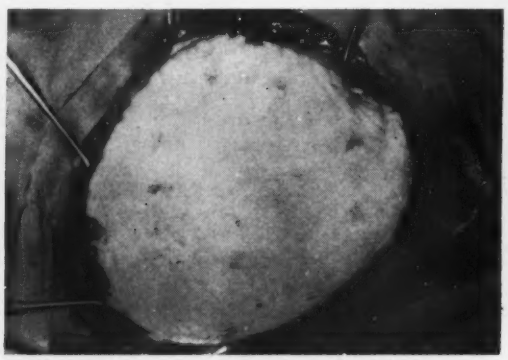

Figure 1. Abdominal wall defect (14 by 24 cm.). Bowel retained by abdominal tape.

Figure 2. A two-layer closure of defect with Fiberglas prosthesis.

der, was excised en bloc. The remaining portion of the bladder was closed with a 2-0 chromic running suture and the suture line was peritonealized. The bladder was drained by a Foley bag catheter. This portion of the operation was done by Dr. T. G. Orr, Jr. A double layer of Fiberglas was used to close the defect (14 by 24 cm.) (Figures 1 and 2). Fixation was accomplished by interrupted 4-0 black silk and a peripheral continuous running steel suture. A large abdominal flap was raised, based laterally on each flank extending superiorly below the breast fold and inferiorly to the margin of the surgical defect. The elevated flap was moved distally to cover the Fiberglas prosthesis. The area of the lower chest wall and upper abdomen was covered with split thickness skin grafts (Figures 3 and 4). A Penrose drain was placed retropubically in the mid-line down to the peritoneum. Pathological diagnosis: a mucinous adenocarcinoma of the urachus. The postoperative course was stormy and complicated by electrolyte problems superimposed on an arteriosclerotic kidney. The patient died on August 17, 1952, from the effects of a vesico-perineal fistula, peritonitis and bronchopneumonia.

Comment: This huge defect lent itself to an easy closure by means of Fiberglas. A bipedicle flap carrying its own blood supply is necessary to provide coverage for any inert foreign prosthesis. Although this patient died from the effects of peritonitis from a vesico-peritoneal fistula, the above outlined procedure points the way to handling extensive abdominal wall malignancy. At the time of postmortem, minimal fibrinous adhesions were present between the bowel and the Fiberglas.

SUMMARY

Fiberglas fabric provides another material for the surgeon in repairing massive defects of the abdominal wall. It is well-tolerated and easily fashioned to fit the particular needs of the moment. Even when replacing the peritoneum, no difficulty was encountered.

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Figure 3. Right side of operative field showing migrated flap and split skin graft closure.

Figure 4. Repaired left side of field. Long silk sutures were tied over a stent dressing for added fixation of split grafts.

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The Treatment of Hyperthyroidism with Radioactive Iodine, I^{131}

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The radioactive isotopes of iodine have been used as diagnostic and therapeutic agents in thyroid disease since 1938.[1, 2] Several isotopes have been used, but the longer half-life of I^{131} (eight days) has made it the agent of choice. More than three thousand reported cases of thyrotoxicosis have been treated with radioiodine, and the results indicate remission of thyrotoxicosis in approximately 96.5 per cent.

Following ingestion of any inorganic salt of iodine, the substance is absorbed nearly completely, and varying amounts are removed from the blood stream by the thyroid gland for use in the synthesis of thyroid hormone. Virtually all the remainder is excreted in the urine within 48 hours. The thyroid gland is capable of accumulating inorganic iodine in a concentration ten thousand times that of blood or any other tissue. The radioactive isotopes of iodine apparently are absorbed, metabolized and excreted in the same manner as the common form of the element. Such isotopes, moreover, can be followed in their course through body tissues because of their radioactivity.

The amount of I^{131} taken up by the thyroid gland varies in direct proportion to the activity of the gland at the time of administration. After ingestion of a tracer dose of I^{131}, the thyroid gland of the euthyroid individual will concentrate between 10 and 40 per cent of the dose given at the end of 24 hours. Patients with myxedema show uptake values below 10 per cent (as low as 0 per cent) and hyperthyroid patients show uptake rates above 45 per cent. Uptake rates may be estimated by the amount of gamma radiation measured by a Geiger-Mueller counter over the thyroid area compared with the radiation from an aliquot of the same tracer material used after background counts are subtracted.

I^{131} emits two forms of energy during its disintegration process, gamma rays and beta particles. The gamma emanations are non-particulate electromagnetic rays behaving exactly like x-rays in all physical respects, and as such they penetrate relatively great thicknesses of matter. Beta particles, on the other hand, have definite physical mass, dimensions and electrical charges, all of which properties restrict their ability to penetrate matter. Consequently, the beta particles of I^{131} dissipate all their kinetic energy within an average radius of 2 to 3 millimeters from their point of origin, while the gamma rays may penetrate many centimeters of matter or tissue with only partial loss of their total potential of energy and contribute only approximately 10 per cent of the total radiation effect to the thyroid area and a negligible amount to surrounding structures. Thus, the majority of the therapeutic effects of radioactive iodine are produced by the beta particles.

This explains why doses of radiation estimated at approximately 10,000 roentgens equivalent physical can be delivered to the thyroid cells without appreciable radiation effects to surrounding structures. For example, the parathyroid glands are effectively shielded from the beta particles by the thin capsule surrounding them, and other contiguous structures in the neck escape damaging radiation effect. A single case of temporary hypoparathyroidism has been reported following radioiodine therapy.[3] Hypocalcemic tetany occurred in this case, a 14-year-old boy, 10 weeks after a therapeutic dose of 4 millicuries of I^{131}. No other cases have been reported to our knowledge, even in thyroid carcinoma where very large

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doses are given and depression of bone marrow and ovarian function has been observed.

The gamma rays, however, by virtue of their ability to penetrate matter, make possible the measurement of radioactive iodine in tissues since they can be detected at considerable distances by means of the Geiger-Mueller counter.

METHODS AND MATERIAL

Since May, 1950, 121 patients have been treated with I^{131} at the University of Kansas Medical Center. Of these, nine patients were treated for carcinoma of the thyroid gland without hyperthyroidism; one patient had heart disease and no hyperthyroidism; the remaining 111 patients were considered to have thyrotoxicosis after clinical appraisal. Fifty of these have been followed for periods varying from 6 to 26 months, and they form the basis of this report. The remaining 61 patients have been treated within the six-months period immediately prior to this report or have been lost to follow-up. Ages of the 50 patients followed six months or longer ranged from 19 to 73 years. Forty-five were above 35 years of age.

Various objective tests of thyroid function were made in each case, including basal metabolic rate, serum cholesterol, serum protein-bound iodine, and I^{131} uptake rate, although all of these studies were not done in each patient. The final diagnosis of hyperthyroidism was based on the clinical impression in conjunction with laboratory procedures. I^{131} uptake studies were done in each case before treatment and at varying intervals following treatment.

A simple direct counting method was used in determining the percentage uptake of I^{131}. The count from a conventional Geiger-Mueller tube 19 centimeters from the patient's thyroid, 24 hours after administration of a 0.050 millicurie tracer dose, was compared to the count of an identical 0.050 millicurie sample after room and biological background corrections were made. From observations early in our experience with I^{131}, excretion studies and effective half-life determinations were found to contribute no additional accuracy in uptake studies or therapeutic management of hyperthyroidism. This does not apply to carcinoma of the thyroid.

Hospitalization is not necessary in carrying out diagnostic or therapeutic procedures with I^{131}, and the majority of patients were treated on an ambulatory basis as outpatients.

The determination of an optimal dose of I^{131} for a given patient is one of the major problems in this type of treatment.[8] In the surgical treatment of the diffuse toxic goitre, many authorities believe that as much thyroid tissue as possible should be removed, leaving only enough to insure preservation of the parathyroid glands. In clinics where this attitude prevails, the incidence of postoperative recurrent hyperthyroidism is effectively reduced, but the incidence of myxedema increases. If this attitude of near-total ablation of thyroid tissue were applied to I^{131} therapy in diffuse toxic goitre, then excessive dosage could be administered and the necessity for re-treatment could be reduced, but myxedema could be expected to occur more commonly, and other tissues of the body would be subjected to an increased danger of radiation effect.

By attempting to calculate the optimal dosage according to uptake rate, gland size, and retained dose per gram of thyroid tissue, a fairly satisfactory estimate can be made in the majority of cases. Other methods of calculation involving considerations of effective half-life are time-consuming and do not seem to contribute to accuracy. At present, our plan is to administer a dose which will result in a retained amount of 0.120 to 0.150 millicuries per estimated gram of thyroid tissue in diffuse toxic goitre, and 0.250 to 0.300 millicuries per gram to the nodular toxic goitre. Inexperience and a conservative attitude caused us to use less than optimal dosage in many of the earlier cases. Consequently, retreatments are more numerous in these patients.

RESULTS

In the group of 82 patients followed for at least two months after one or more treatments, remission of thyrotoxicosis occurred in 79 patients (96 per cent) (Table 1). When the group is limited to those with six months or more follow-up, remission occurred in 48 of 50 patients (96 per cent) (Table 2). One patient was clinically euthyroid at two months following therapy, at which time she showed 10 per cent uptake of a tracer dose of I^{131}. Three months later, she was clinically in a recurrent state of hyperthyroidism and showed an uptake rate of 37 per cent. She was re-treated with good results.

TABLE 1

THERAPEUTIC RESULTS WITH I^{131} IN 111 CASES OF HYPERTHYROIDISM

Remission of thyrotoxicosis		79
Followed 2 months	9	
Followed 2 to 6 months	23	
Followed 6 to 12 months	17	
Followed 12 to 27 months	30	
Total	79	
Unsatisfactory results		3
X-ray therapy 2 months following I^{131} treatment	1	
Thyroidectomy 8 months following I^{131} treatment	1	
Thyroidectomy 12 months following I^{131} treatment	1	
Total	3	
Results not evaluated		29
Less than 2 months follow-up (recently treated)	19	
Lost to follow-up	10	
Total	29	
Total		111

TABLE 2

RESULTS IN 50 PATIENTS FOLLOWED FOR 6 TO 27 MONTHS

	Patients No.	%
Clinically Euthyroid	41	82
Clinically Myxedematous	7	14
Treatment Failure*	2	4
	50	100

* Both patients underwent thyroidectomy within 12 months following I^{131} therapy.

This is the only patient in the entire group in whom an I^{131} uptake below 20 per cent was recorded at the two-months post-treatment period and who later showed a recurrence of hyperthyroidism. Clark et al,[4] in reporting I^{131} therapy in 384 cases of thyrotoxicosis with 6 to 60 months follow-up, found no case of recurrent hyperthyroidism in patients who had been observed to be in a remission for four months after treatment.

Total doses in this group ranged from 3 to 29 millicuries in the diffuse goitres, with an average dose of 10.5 millicuries. Our experience with toxic nodular goitre has been similar to the published experience of others.[4, 5, 6, 7] In these patients, the dose varied widely and the necessity for re-treatment was more common. The six cases of nodular toxic goitre required from 9 to 67 millicuries total dosage, the average being 29 millicuries.

When the size of the initial dose of I^{131} is compared to the results obtained (Tables 3 and 4), approximately one-third of the patients receiving less than 10 millicuries as an initial dose, or less than 0.140 millicurie per gram of estimated thyroid weight, did not show a sustained remission of thyrotoxicosis. Slightly more than one-fourth of the patients receiving more than 10 millicuries, or more than 0.140 millicurie per gram of thyroid weight, have become myxedematous.

TABLE 3

RELATION OF SIZE OF INITIAL DOSE (MILLICURIES PER GRAM) TO RESULT

Initial Dose in mc/gram of Thyroid Tissue	Euthyroid	Hypothyroid	Total Remissions	Required Re-treatment
Less than 0.100	45%	11%	56%	44%
0.100-0.140	65%	8%	73%	27%
0.140-0.180	40%	40%	80%	20%
Over 0.180	84%	16%	100%	0%

TABLE 4

RELATION OF SIZE OF INITIAL DOSE TO RESULT

Initial Dose in millicuries	Euthyroid	Hypothyroid	Total Remissions	Required Re-treatment
3 - 6	40%	15%	55%	45%
7 - 10	81%	6%	87%	13%
11 - 17	76%	12%	88%	12%
18 - 27	67%	33%	100%	0%

It is frequently difficult to classify accurately the recurrent goitre as either "diffuse" or "nodular" toxic goitre. When thyrotoxicosis recurs following thyroidectomy, the regrowth of thyroid tissue is apt to occur in a nodular fashion. This type of gland, however, cannot be considered as identical with the toxic adenoma so far as its response to I^{131} therapy is concerned. Our series of recurrent toxic goitres is too small to permit any conclusions, but it is our impression that they should be dealt with as diffuse toxic goitres.

In a number of patients, post-treatment observation at two to four months revealed clinical evidence of mild to moderate myxedema, and in 19 patients the I^{131} uptake values were in the myxedema range (below 10 per cent). Fourteen of the 19 recovered from this transient hypothyroid state and were considered euthyroid when last seen. Seven patients were considered to be clinically hypothyroid after six months or more follow-up. Comparison of the clinical appraisal of the patients to the I^{131} uptake rate is presented in Table 5. We feel that thyroid extract should not be administered to patients showing post-treatment hypothyroid states unless they fail to recover from severe myxedema after eight months observation, since it has been shown that administration of thyroid extract tends to depress thyroid activity. There is no evidence in this series that re-treatment increases the incidence of myxedema. In the patients receiving more than one treatment, 13 per cent were considered hypothyroid after remission of thyrotoxicosis; in those receiving only one dose of I^{131}, the incidence of hypothyroidism was 14 per cent.

TABLE 5

CLINICAL APPRAISAL COMPARED WITH FOLLOW-UP I^{131} UPTAKE RATE 6 TO 27 MONTHS AFTER LAST TREATMENT

I^{131} Uptake	Euthyroid No.	%	Myxedema No.	%
Below 10%	5	10	3	6
10 to 35%	28	56	0	0
Not tested	8	16	4	8
	41	82	7	14

Exacerbation of the thyrotoxic state in the immediate post-treatment period ("thyroid storm") has been reported following I^{131} therapy.[9] This was observed in a mild form in one of our patients, but required no specific therapy other than barbiturates and subsided within a few days. A few patients have complained of slight tenderness over the thyroid gland in the immediate post-treatment period. This reaction is, perhaps, due to a mild form of irradiation thyroiditis.

Exophthalmos was present in 29 of 111 cases (27 per cent). Seventeen of these cases have been followed at least six months. Seven have shown marked improvement in the exophthalmos; slight improvement occurred in four, and no change was observed in six. None of these cases without exophthalmos have developed it following treatment, and there has been no exaggeration of already existing exophthalmos.

Failure of a single treatment to produce a satisfactory remission should not be considered as a treatment failure, but rather both physician and patient should be aware at the outset that one or more retreatments might become necessary in order to bring about a sustained remission. This is especially true in nodular toxic goitre. One can hope that further experience will reduce the necessity for more than one treatment. Follow-up observations should be made at specified periods following treatment. Our present plan is to re-evaluate the patient clinically and by I^{131} uptake rates at two months and six months after treatment and then annually. If a remission has not occurred, retreatment is administered, the dosage being calculated in the same manner as at the original treatment.

Of the three patients listed as treatment "failures," one was still in a hyperthyroid state two months following therapy, at which time x-radiation was administered rather than re-treatment with I^{131}. The second patient had bronchiectasis and had had lipiodol instilled into the bronchial tree prior to treatment with I^{131}. Perhaps because of the lipiodol, the I^{131} uptake was only 24 per cent. After two attempts to treat her with I^{131} in spite of the low uptake, she remained in a hyperthyroid state and underwent thyroidectomy. The third patient had a large nodular gland with substernal extension. She had received Lugol's solution until one month prior to admission to the University of Kansas Medical Center, at which time she showed 14 per cent uptake of a tracer dose of I^{131}. She was given a therapeutic dose of 20 millicuries of I^{131} which probably delivered less than 0.010 millicurie per gram of thyroid tissue. She continued in a hyperthyroid state, and thyroidectomy was performed elsewhere approximately 12 months later. The dosage was much too low to expect a good result in the latter two cases, and the clinical situation demanded effective control of the thyrotoxicosis without further delay. These cases illustrate the fact that failures will occur in I^{131} therapy in cases showing unmistakable evidence of thyrotoxicosis in whom the I^{131} uptake rate has been depressed to low levels by recent administration of iodine-containing medications or diagnostic contrast media, such as lipiodol or the substances used in cholecystography and urography.

If antithyroid drugs have been administered prior to treatment, they should be interrupted for seven days before a tracer study is done. These compounds should not be administered in the immediate post-therapy period since they are known to increase hormone release from the thyroid gland and consequent reduction of I^{131} content. In severely toxic patients where immediate control of thyrotoxicosis is imperative, antithyroid drugs may be administered beginning on the sixth post-treatment day. As thyrotoxicosis comes under control, the antithyroid medication should be gradually withdrawn. We have noted clinical improvement to occur usually between four and six weeks, and believe maximal I^{131} effect to be present at eight weeks. In the few cases in this series that were given post-I^{131} therapy antithyroid medication, the drug was discontinued before six weeks had elapsed.

SUMMARY

1. One hundred eleven patients with hyperthyroidism were treated with I^{131} at the University of Kansas Medical Center during the period from May 1, 1950, to December 31, 1952. Fifty of these patients have been followed at least six months since their last treatment.

2. Remission of thyrotoxicosis occurred in 96 per cent of the group with at least six months follow-up.

3. Clinical myxedema occurred in 14 per cent of patients.

4. Failure of treatment in two patients (4 per cent) is attributed to previous administration of iodine-containing materials. Attempts at I^{131} therapy were ill-advised in these patients.

5. I^{131} uptake rates below 20 per cent at the two months follow-up period predicted sustained remission of thyrotoxicosis in all but one patient.

6. Re-treatment is frequently necessary and apparently does not increase the incidence of post-treatment myxedema.

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PRESIDENT'S PAGE

DEAR DOCTOR:

We have been much interested in reading about changes which are proposed for the Taft-Hartley Act. It seems that the present act is to be completely worked over. Mr. Taft himself has introduced five bills which include sixteen proposed changes. Others will be added, no doubt, to swell the total.

There are some conclusions which seem to be in order from the ordinary citizen's viewpoint. They may have some value and they seem not to be entering too much into the thinking of the principals in the matter.

The first of these is that apparently the government has maneuvered itself into a position whereby it is obliged to enforce laws which would protect labor leaders who have, in effect, usurped the powers of government. Whether these powers have been usurped or granted makes little difference—the fact remains that under such laws a labor leader has the right to force the nation to submit to his wishes, even when such action might mean unemployment on a mass basis. Since force is not an ingredient of democratic government and, except in rare instances, should have no part in democratic rule, this is not an enviable position for the government of a democracy to have to assume.

The second observation is that in arriving at such an impasse in labor matters our experts have once again lost sight of certain fundamental concepts which are guaranteed by the Constitution, which have been accepted as part of the American tradition, and which are, we think, the answer to all labor-management disputes.

In a democracy no one has the right to tell a person when he can or cannot work without first obtaining his consent to such an agreement. This principle was accepted in America with the abolition of slavery.

In a democracy an individual's abilities are properly his own personal property and as such cannot be encroached upon by another party without his consent. Every individual has the right to dispose of his abilities as he sees fit, i.e., in an open and free market.

The only price that can honestly be put upon one's labor is what that commodity will bring in the free market. Any other mechanism to raise or lower a commodity is artificial, unnatural, and immoral.

We believe that the only fair and honest answer to the question of labor-management problems and even the settlement of strikes is the application of the principle of the rights of the individual as set out in the Constitution and the resumption of the operation of the free market.

EDITORIAL COMMENT

Salute to Medical School

This, the Seventh Annual University of Kansas School of Medicine issue of the JOURNAL, is offered as a salute to our state medical school. Although a recognition tendered for the seventh consecutive year might seem to have become routine, in this case it is not. It is a sincere tribute to an organization that is progressive, alert, and successful in the ideals to which it is dedicated.

It is unnecessary now to report on progress made in recent years since an article on the subject by Dr. W. Clarke Wescoe, dean of the school, was published in the February issue of the JOURNAL. That article dealt with increased enrollment, expansion of the postgraduate education program, activities in research, and needs of the immediate future.

The University of Kansas School of Medicine, which has inaugurated programs that have been copied throughout the country, is an object of pride for citizens of this state. It has received wide recognition from the press and from professional and non-professional individuals and groups. The JOURNAL welcomes the opportunity of adding its congratulations and encouragement by devoting this issue to the school.

In the scientific section there are papers from the following departments: radiology, cardiovascular studies, pediatrics, internal medicine, surgery, and pathology. In addition, the school has provided a case report that was the subject of a clinical pathological conference and a thesis written by one of the senior students. Dr. Glen R. Shepherd, assistant to the dean, in his capacity as an associate editor of the JOURNAL, assembled the material for the issue.

Annual Meeting, May 3-7, 1953

The annual session of the Kansas Medical Society, to be held at the Forum at Wichita, May 3-7, promises to be an outstanding event since it will mark two occasions, the 94th anniversary of the state society and the 50th anniversary of the host group, the Sedgwick County Medical Society.

Committees in Wichita have been working for months to plan a scientific program and a schedule of entertainment that will be of interest to all. Chairmen of the different groups are as follows: General Chairman, Dr. Edward S. Brinton; Scientific Program, Dr. James B. Fisher; EENT Program, Dr. Norton L. Francis; Entertainment, Dr. Lester K. Nix; Reception, Dr. Lloyd P. Warren; Commercial Exhibits, Dr. Robert K. Purves; Scientific Exhibits, Dr. Bert E. Stofer; Publicity, Dr. Donald P. Trees; Auxiliary, Dr. William H. Browning.

The scientific program, which makes up the foundation for the annual meeting, will include guest speakers who are outstanding in their specialties. Separate sessions will be held for those practicing in the EENT specialty only. The list of scientific speakers includes the following: Dr. Charles P. Bailey, Philadelphia, thoracic surgery; Dr. Elmer Belt, Los Angeles, urology; Dr. Arthur C. Curtis, Ann Arbor, dermatology and syphilology; Dr. Harold L. Hickey, Denver, ENT; Dr. C. Gordon Johnson, New Orleans, obstetrics and gynecology; Dr. Peter C. Kronfeld, Chicago, ophthalmology; Dr. Frank R. Lock, Winston-Salem, obstetrics and gynecology; Dr. Edward B. D. Neuhauser, Boston, radiology; Dr. William D. Robinson, Ann Arbor, medicine; Dr. Edward H. Rynearson, Rochester, medicine; Dr. R. L. Sanders, Memphis, surgery; Dr. Hugh Smith, Memphis, orthopedic surgery; Dr. Orvar Swenson, Boston, pediatric surgery.

The annual banquet on Wednesday evening, May 6, will be the most important social event of the session. An elaborate program is being prepared. Other features of the meeting are sports events for golfers and marksmen, a tournament banquet, scientific movies and exhibits, commercial exhibits, meetings of specialty groups, and two meetings of the Society's House of Delegates. The Kansas Medical Assistants' Society will hold its annual convention on May 3 and 4, and the Woman's Auxiliary to the Kansas Medical Society will meet on May 5 and 6.

An innovation this year will be a health forum for approximately 5,000 invited guests who are not members of the medical profession. The program will be presented in the Forum, and the guests will be permitted to view the scientific and commercial exhibits as they enter the building. This plan, devised as a public relations project, is expected to be a popular feature of the meeting.

Members of the Kansas Medical Society are urged to make hotel reservations immediately by writing directly to the hotel of their choice in Wichita. The larger hotels there are the Allis, the Broadview, and the Lassen. It is believed that accommodations will be available for all who wish to attend, but only those who make early reservations will be assured of the desired type and location of rooms.

The Promise of Gamma Globulin

The development of a practical preventive for poliomyelitis, featured prominently in the lay press in 1952, has been evaluated for the medical profession by the National Foundation for Infantile Paralysis. Although optimistic about the probability of finding a safe, sure, long lasting immunizing agent

some time in the future, the Foundation refers to its 1952 experience with gamma globulin as "a beginning in the development of a practical preventive."

Among significant research findings during the year, according to the Foundation, was the discovery by Dr. Dorothy Horstman of Yale and Dr. David Bodian of Johns Hopkins that poliomyelitis virus could be found in the blood stream of cynomologus monkeys and chimpanzees four to six days after they had been fed polio virus. This research showed that during the brief viremia phase, antibodies were developed in the blood. In a few animals sufficient antibody developed to prevent paralysis. In others, the amount of antibody was either insufficient or its development was too slow to ward off paralysis. However, by slightly increasing the amount of antibody present in the blood, paralysis could be prevented until the animal had time to develop its own active immunity.

Viremia in human beings has been observed on only two occasions. Yet it was felt that because of the similarity between the laboratory disease in animals and the naturally acquired disease in man, it might also be a constant part of the human disease picture that polio virus regularly circulates in the blood a week or more before the onset of paralysis. If this were true, by giving antibodies to human beings just prior to or just after infection, it might be possible to prevent the development of paralysis.

This hypothesis was tested during polio epidemics in Utah, Texas and Iowa, with 54,772 children between the ages of one and eleven taking part. Half received injections of gamma globulin and half an innocuous substitute. Gamma globulin containing antibodies against all three immunological types of polio virus was obtained from the American National Red Cross and was prepared from blood collected during World War II from tens of thousands of donors in different areas of the country.

A preliminary report was issued by Dr. William McD. Hammon of the University of Pittsburgh Graduate School of Public Health, who conducted the study. Ninety paralytic cases developed among the 54,772 children. Twenty-six cases occurred in children who received gamma globulin injections, with 64 from the other group. The figures emphasize that marked protection did not begin until the second week after inoculation, lasting through the fifth week. During the second week, the number of polio cases in the gamma globulin group was three; in the control group, 23. From the second week through the fifth week, only six cases occurred in the gamma globulin group, while 38 appeared in the control group.

In the first week little, if any, protection was observed. However, the cases were mild, and within 30 days half had completely recovered. Dr. Hammon believes this indicates that gamma globulin may, during the late stages of the incubation of polio, modify the severity of the disease although it fails to give complete protection.

This preliminary report points up two needs for the future, the securing of large amounts of gamma globulin and the continuation of research on the disease. Both projects are currently receiving attention with the hope that ultimately the disease, which struck 1,716 victims in Kansas in 1952, will be conquered.

Annual Mid-West Cancer Conference

Plans are now being completed for the Fifth Annual Mid-West Cancer Conference to be held at the Broadview Hotel, Wichita, April 2 and 3. Scientific sessions will fill both days, and an informal dinner meeting will be held on Thursday evening, April 2. Dr. Charles H. Miller, Parsons, will preside at the dinner, and Dr. Cornelius P. Rhodes, New York City, will speak on "Horizons in Cancer Research."

The scientific program will be presented by the following guest speakers: Dr. William Boyd, University of British Columbia, Vancouver, B. C.; Dr. Paul C. Bucy, professor of neurology, University of Illinois College of Medicine; Dr. Ernest M. Daland, chief of staff of Pondville Hospital, Walpole, Massachusetts; Dr. Juan A. del Regato, director of Penrose Cancer Hospital, Colorado Springs; Dr. Cushman D. Haagensen, associate professor of clinical surgery, Columbia University, New York; Dr. Henry S. Kaplan, professor of radiology, Stanford University Hospitals, San Francisco; Dr. Cornelius P. Rhodes, director of Memorial Hospital, New York; Dr. Isidore Snapper, director of medical education, Mt. Sinai Hospital, New York.

Dr. Karl E. Voldeng, Wellington, will preside at the Thursday morning program, which will begin at nine o'clock and continue as follows:

A Concept of Cancer ..... Dr. Boyd
Research in the Chemical and Biological Therapy of Cancer ..... Dr. Rhoads
Clinical Management of Lymphomas and Leukemia ..... Dr. Kaplan
The Treatment of Cancer of the Skin ..... Dr. del Regato

During a luncheon session, with Dr. J. P. Berger, Wichita, presiding, motion pictures on cancer subjects will be shown.

On Thursday afternoon Dr. Richard E. Speirs, Dodge City, will preside at the following program:

Early Signs and Symptoms of Brain Tumors ..... Dr. Bucy
The Spread of Tumors ..... Dr. Boyd
Cancer of the Lip, Tongue, and Jaw, Dr. Daland

Tumors of the Spinal Cord and Their Differentiation from Degenerative Lesions, Dr. Bucy

A symposium on cancer of the breast will make up the program on Friday morning. Dr. Willard J. Kiser, Wichita, will preside. The following papers will be given:

The Diagnosis of Tumors of the Breast ..... Dr. Haagensen
The Role of Radiotherapy in the Treatment of Cancer of the Breast .... Dr. del Regato
The Treatment of Breast Carcinoma ..... Dr. Haagensen
The Palliative Treatment of Carcinoma of the Breast ..... Dr. Daland

Dr. Larry E. Vin Zant, Wichita, will preside at the Friday luncheon meeting, and Dr. Horace M. Wiley, Garden City, will preside in the afternoon. The program to be given includes:

Endocrinological and Metabolic Changes Following Castration and Testosterone Treatment for Breast Cancer ..... Dr. Snapper
Panel Discussion and Question Period on Cancer of the Breast ..... Dr. Daland, Dr. del Regato, Dr. Haagensen, Dr. Snapper
The Diagnosis of Cancer in the Gastrointestinal Tract ..... Dr. Kaplan
Recent Advances in Treatment of Multiple Myeloma and Other Malignancies .. Dr. Snapper

Kansans Guests at Richmond Conference

Dr. and Mrs. Henry E. Haskins of Kingman will be Kansas' guests of honor at the First Western Hemisphere Conference of the World Medical Association, to be held in Richmond, Virginia, April 23 to 25, 1953, in observance of the lengthening of life and the constant improvement of human health.

Governor Edward F. Arn nominated Dr. and Mrs. Haskins for the honor of attending, at the invitation of Governor John S. Battle of Virginia. The governor of each state was asked to appoint a physician who will reach the age of 75 during 1953. During the conference each physician will tell of medical advances that have taken place during his lifetime.

Dr. Haskins has been in general practice for more than 50 years, beginning his medical service immediately after graduation from the Beaumont Hospital Medical College, St. Louis, in 1901. He was born in 1878, the year Robert Koch published his history-making treatise on causes of infection.

Dr. Louis H. Bauer, president of the American Medical Association, will greet the guests at the Richmond conference, and other addresses will be given by leaders of Latin American medical societies. The program will also include scientific sessions and tours of historic sites in Virginia. All expenses of the conference are covered by a grant from A. H. Robins Company, Inc., Richmond pharmaceutical house founded 75 years ago.

"Alcohol is involved in thousands of deaths, the official records of which make no reference to it," the American Business Men's Research Foundation reported recently in making public a study of vital statistics records. The records, according to the foundation, show that in 67 varieties of disease alcoholism has been found to be a factor.

SERVICE SEPARATIONS

As a service to physicians and communities in this state desiring additional medical personnel, the Journal of the Kansas Medical Society will publish in this column each month the names of medical officers who will shortly be separated from the armed forces. These are men who volunteered from Kansas, and many of them will probably be interested in finding locations in this state. Anyone interested in contacting these physicians may write to the address here given.

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Clinical Pathological Conference*

CASE PRESENTATION

This was the first KUMC admission for this 23-year-old white man. Chief complaints were "spells" for two and one-half years, "weakness" for one month, and "stomach hurts" for one week.

The present illness began suddenly in February, 1950, with a tingling sensation from the waist up, followed by ability to hear people talk to him but inability to answer, for at least two or three minutes; then, when able to talk, the speech was irrelevant and disjointed. The patient had two to three such attacks per week.

In March, 1950, he was seen in the outpatient department. During this examination the patient had an episode of unresponsiveness with grimacing and flexion of the right arm in tonic contraction. On recovery there was a period of five minutes when speech was irrelevant and a five-minute period of retrograde amnesia, but no post-seizure sleeping.

Physical examination at this time was negative except for absent right abdominal reflexes. An EEG done at this time revealed diffuse disturbance in cerebral cortical rhythm with right temporal parietal preponderance.

The patient was then placed on anti-convulsive medications with varying success. During the ensuing year seizures increased in frequency and intensity, and consisted of aura, blurring of vision, weakness, occasional unconsciousness, and unilateral right-sided convulsive movements.

The patient's family reported urinary incontinence and unilateral left-sided perspiring with these seizures, which showed a wide variation in severity. Six weeks before this admission the patient had virus pneumonia and was given chloromycetin, and during this time he was free of the attacks while hospitalized.

In the past month there had been an increase in seizures, with two to three occurring daily. All had been accompanied by loss of consciousness and minimal right-sided convulsive movements. There had been a continuous increase in fatigability and muscular weakness. For the week previous to admission the patient had complained of mid-abdominal pain of a dull, constant nature.

The past history was non-contributory, although the patient had had a blow to the right occiput with unconsciousness but no sequelae at age eight, and an appendectomy in 1951.

The family history was non-contributory.

Symptom review revealed nocturnal enuresis twice in the past two months and a present diffuse aching about the knees and elbows with their movement.

Physical examination showed a tall, thin individual who appeared the stated age but did not appear either acutely or chronically ill. Blood pressure was 120/80, pulse 96, temperature 99.4, respirations 20. Head examination was not remarkable. The fundi were negative. The neck was not remarkable, and the chest was clear to percussion and auscultation. The heart presented a regular sinus rhythm without murmurs and was not enlarged. Neither the abdomen nor the extremities were remarkable. Neurological examination was negative except for an intermittently absent right abdominal reflex.

Laboratory data: Urinalysis—acid, 1.017 sp. gr., faint trace of albumin, occasional granular casts, 3 to 4 WBC per high power field, no sugar. Complete blood count showed 5,000,000 RBC, 9,000 WBC, 14.2 gms. hemoglobin and a differential count of 86 per cent polys., 8 lymphocytes and 6 monocytes. Serology was negative. Blood chemistry showed the NPN 33, creatine 1.3, sugar 75 mgm. per cent. The glucose tolerance curve was normal. Heterophile agglutination was positive in 1 to 4 dilution. Skin tests showed tuberculin negative, histoplasmin positive, blastomycin negative and coccidioidin negative. Spinal fluid examination showed no cells, sugar 72, chloride 750, serology negative, protein 34 mgm. per cent, and culture negative. Urine culture showed a moderate growth of pseudomonas. Sputum cultures revealed no acid fast bacteria, while the nose and throat cultures showed only the usual flora. Routine agglutinations were negative in all dilutions. Blood cultures were negative in 10 days.

Following admission, the patient was taken off anti-convulsive medication until after an electroencephalogram was done. During this period, the patient had 5 to 15 mild epileptic episodes, each of one to two minutes duration, during which there was unresponsiveness, flickering of the eye lashes, and at times a withdrawing of the right arm and sometimes the leg. The patient stated that he was not unconscious during these periods but simply could not respond. A low-grade fever continued following admission.

On the ninth day after admission an exploratory craniotomy was done. The immediate postoperative course was smooth and the patient responded. On the tenth hospital day the patient became unresponsive, and a ventricular puncture was done. The patient responded but was disoriented. Intermittent periods of central nervous system irritability and depression occurred. Postoperative therapy consisted

* From the University of Kansas Medical Center. Edited by Glen R. Shepherd, M.D., and Mahlon H. Delp, M.D., from recordings of the conference participated in by the Departments of Medicine, Neurosurgery, Pathology, and Radiology, and the junior and senior classes of medical students.

of close nursing care, caffeine sodium benzoate, and parenteral fluids.

The patient remained febrile. The temperature spiked to 105°, blood pressure started falling, and the patient became unresponsive and expired at 6:30 on the 13th hospital day.

Dr. Mahlon Delp (Medicine): Any questions of Dr. Gunn?

Question: Were there any personality changes noted at all during his illness?

Dr. C. G. Gunn (Resident in Medicine): None were noted.

Question: Was the spinal fluid pressure recorded?

Dr. Gunn: It was initially 240 mm. After 10 cc. of fluid was removed, it fell to 125 mm.

Question: In the recumbent position?

Dr. Gunn: Yes.

Question: Was this patient righthanded or lefthanded?

Dr. Gunn: Righthanded.

Question: Was there any history of infection at the onset two and a half years ago?

Dr. Gunn: No.

Question: Was a pneumoencephalogram done?

Dr. Gunn: Yes.

Question: Was the ventricular puncture bloody?

Dr. Gunn: No.

Question: Did the patient have any muscle weakness during his neurological examination?

Dr. Gunn: None.

Dr. Delp: Dr. Tice, may we see the x-rays?

Dr. Galen M. Tice (Radiology): Chest films and fluoroscopy were normal in all respects. Examination of the esophagus, stomach and duodenum using a barium meal, fluoroscopy and spot films, showed nothing unusual. Routine films of the skull didn't tell much. They did not reveal evidence of increased pressure or abnormal calcification. An arteriogram was done of the left side. This is the most revealing film. It shows the vessels displaced away from the base of the skull farther than they should be.

This ventriculogram film is, I think, our most important film. It shows displacement of the ventricle to the right, localizing the lesion on the left side. By putting these two together it is obvious that there was a space-taking mass on the left side, in the temporal area.

Dr. Delp: Mr. Billingsley?

DIFFERENTIAL DIAGNOSIS

Mr. Thaine E. Billingsley (Senior Student): The history of this patient makes me want to know three things: (1) What was the disease? (2) Where was the disease? (3) Why did the patient die?

The x-rays show an intracranial space-taking lesion. I'll mention briefly some of the diagnostic possibilities.

A localized meningitis could result in a history very much like this patient had. A subdural hematoma could very doubtfully exist for two and one-half years. Meningeal vascular syphilis is uncommon in the presence of negative blood serology and negative spinal fluid. A gumma is sometimes found in the absence of serological and spinal fluid changes. I think it would have to be seriously thought of, but I don't think this patient's disease was syphilitic.

Cerebral hemorrhage can be found in the young adult. However, the onset in this case was not typical of that. That is true also of cerebral embolism and cerebral thrombosis. With gradual progression of symptoms, one would not think of thrombosis.

Tuberculoma may be found in the absence of any signs of tuberculosis.

Schistosoma japonicum can cause granulomatous brain lesions. We have no history of his having been in the Far East, so I mention that only in passing.

Lead poisoning can produce convulsions, but there is no history of lead exposure. I believe this patient was a farmer and probably did not have any opportunity of developing lead poisoning.

A hemangioma would be present from birth, would probably produce an audible bruit, and probably would not be progressive, so we can rule that out.

Idiopathic epilepsy must be thought of in any type of convulsion, but these were definitely focal convulsions. They began at rather a late age for idiopathic epilepsy.

The x-rays indicate a space-taking lesion. In my estimation, this all boils down to something like a brain tumor, progressive over a period of two and a half years. This could produce focal seizures. The things militating against brain tumor are the absence of papilledema and the absence of headache. However, both of these may be absent in a brain tumor. I think this patient had a brain tumor.

In differentiating brain tumors, I thought of three types: glioma, meningioma, and metastatic carcinoma. I would like to omit consideration of a metastatic lesion, since it would have been symptomless.

Meningioma typically has a long chronic course. Two and a half years is pretty chronic. Meningioma, in 25 per cent of cases, produces some changes in the bone overlying the meningioma, which we do not have here. This patient did have an injury many years ago—15 years ago—so we have to consider meningioma, but, having considered it, I'll pass on to glioma, which I think he had.

The gliomas are the most common of the brain tumors. They infiltrate widely. I think the symptoms here indicate a widely infiltrating tumor. Certain of them have a very rapid course, but certain others do not.

In thinking of the gliomas, I'd like to mention

first medulloblastoma, which is rare in adults, more common in children, and usually has a more rapid course than in this case.

Glioblastoma multiforme is usually found in persons over 35 years of age, and rarely is found in young adults or children. It is rapidly growing, very malignant, and nearly always produces headache and increased pressure signs, neither of which this patient had.

Oligodendroglioma is a rare tumor, being found in about one per cent of brain tumors. A ten-year course is common, and a two and a half-year course is not at all uncommon. I don't think it can be ruled out in this case because it often begins with epileptic attacks. Increased pressure signs are absent.

I cannot rule out ependymoma or oligodendroglioma.

Regarding astrocytoma, authorities give the average duration of symptoms before the patient sees the surgeon as 31 months. This patient had symptoms for two and a half years. It is the most common of the gliomas—perhaps 35 to 40 per cent of gliomas are astrocytomas—and it is slow growing. Because it is slow growing, the brain adjusts to the extra pressure and there are no signs of intracranial pressure. These tumors infiltrate widely. They even may go from one lobe to another. A widely infiltrating lesion better explains the symptoms this patient had, so I'd like to think that it was an astrocytoma. Such a tumor is most commonly cerebral in location.

Astrocytomas may be either cystic or solid. Solid are most common in the adult. The solid type also infiltrates more widely. Because I need a widely infiltrating tumor to explain the symptoms in this case, I'm going to vote for a solid astrocytoma.

Where was the disease? Obviously, on the left side. Since he was righthanded, I'll put the lesion on the left side of the brain. The patient started with the history of paraesthesias. That would make me think of the possibility of a tumor in the parietal lobe. However, these were connected with a history of aphasia and jargon aphasia. Motor aphasia usually is localized in the frontal lobe anterior to the motor cortex in Broca's area. This patient gives the history of being able to hear people talk but not being able to answer. That sounds like motor aphasia. However, as the patient came out of these attacks, speech was irrelevant, which gives the possibility of jargon aphasia. In jargon aphasia, the lesion quite often is located near the superior temporal gyrus, in the temporal lobe, whereas the motor aphasias are from frontal lobe lesions. One can have jargon type aphasia with a lesion in the frontal lobe. I believe that's what this was. There's the motor aphasia and then, as the patient is regaining the ability to talk, he seems to find words and sometimes substitutes the wrong words until the ability to talk comes back completely.

The outstanding thing about the history in this case, I think, are these focal convulsions. They are described as being a grimace and arm movements. They also would localize the tumor in the frontal lobe down near Broca's area, impinging by pressure or infiltration on the part of the motor cortex which controls the upper part of the body. The fact that he had absent abdominal reflexes, I think, indicates no specific lesion. The specific findings we have indicate a cerebral tumor.

The EEG one and a half years ago localizes the lesion to the right side of the brain. I don't know what the EEG on this last admission showed, but it has been said that the EEG is about useless as far as localization goes. Certainly, you can't throw out the clinical findings because the EEG does not agree with them.

Another thing that I think indicates there may be a frontal lobe tumor here is the fact that stimulation of the frontal lobe in animals produces increase of intestinal peristalsis. In ablation of the frontal lobes, it is said that peristalsis may become so great as to produce intussusception. This patient, after many years of the disease, did give a history of a week of abdominal upset not connected with food. My first guess on that would be a lesion in the frontal lobe causing the abdominal difficulty.

So my best diagnosis is an astrocytoma, localized in the frontal lobe near Broca's area.

The astrocytoma infiltrates widely and is removed by extirpation. It cannot be cured, as I understand it, but it can be helped a great deal by taking it out. I think at the exploratory craniotomy, an astrocytoma was found. It was removed. I think the patient died in one of three ways. He may have had an overwhelming infection, but I don't think so. However, he did have a spiking temperature, so we have to think of that.

He may have had an intracranial hemorrhage. I was hoping that it would be shown that the ventricular fluid was bloody. The intraventricular hemorrhage is described as causing death in about two to four days in a large percentage of cases. Accompanying death there is a hyperthermia, and the patient goes into profound shock and expires. The shock and hyperthermia can be explained as due to irritation of the fourth ventricle. He had those things. However, in the absence of bloody fluid, he probably died of cerebral edema following his operation, possibly due to increase of intracranial pressure producing a herniation down through the foramen magnum. I'm not pleased with that diagnosis, but it's the best I can do as to the cause of death.

CLINICAL DISCUSSION

Dr. Delp: Dr. Stephenson, I would like to establish whether or not you think the electroencephalogram might have been reliable in this patient. In February, 1950, he had an EEG taken, and this report was made: "This is an abnormal EEG with diffuse disturbance of cerebral cortical rhythm. A greater area of dysfunction in the right temporal-parietal triangle strongly suggests possible organic brain disease." What do you think are the implications of that sort of report? How should it be interpreted?

Dr. Wayland Stephenson (Neurology): Judging by the protocol here, this EEG was taken soon after a series of seizures. Any time after a whole series of convulsions of any sort there may be diffuse slowing. Actually, at a time like that we could be very easily confused as to laterality. I think that if the EEG had been made following a period of repose, then we would find it might perhaps have been more localized.

Dr. Delp: You don't think this report indicates that a more extensive examination should have been made?

Dr. Stephenson: I do not think so. The electroencephalographers should not be saddled with that responsibility.

Dr. Delp: Dr. Steegmann, you've seen this patient's clinical examination report. Do you have any comments on the problem, especially covering the two-year period before hospitalization?

Dr. A. T. Steegmann (Neurology and Pathology): The patient was followed in the outpatient clinic. I see no report here of any spinal puncture, and there was a negative skull x-ray. There was a history of these spells beginning before the age of 20. I think that on a statistical basis one might assume that it was not an organic condition. With no family history of epilepsy, this patient probably should have had a pneumoencephalogram at a much earlier date. If a spinal puncture had been done in the outpatient clinic and reported as showing normal pressure and normal spinal fluid findings, with negative skull x-rays, and with EEG findings not inconsistent with the ordinary (idiopathic) type of epilepsy, I still think the diagnosis of brain tumor difficult.

Dr. Delp: You think there's nothing in the history or the signs reported that would not be consistent with epilepsy?

Dr. Steegmann: I think the absence of a family history should always suggest the possibility of a tumor of this type.

Dr. Delp: Dr. Williamson?

Dr. William P. Williamson (Neurosurgery): I think we have to say that these convulsions were focal. Focal seizures are due to a focal lesion of the brain until proved otherwise. We take that as one criterion for our further detailed investigation of convulsive disorders. Another is the age. If the patient starts seizures over the age of 25, it's a brain tumor until proved otherwise. This patient was under 25.

I think these were focal seizures involving the motor speech because during attacks the patient, while unable to talk, still could understand. I think they were focal in their motor component of the motor strip because the arm was involved and the rest of the body was not. Probably the patient had a psychomotor element, which is a focal temporal lobe syndrome, because for five minutes following a seizure there was irrelevance in speech. That may not prove that it was focal because, after such a state, many people will just be confused. But this patient certainly had unusual seizures that pointed to the regions in the left side of the brain in the temporal and low inferior frontal areas.

Before investigation, we asked ourselves, "Is this tumor or is it one of the congenital vascular anomalies?" There is a nonneoplastic situation which produces focal seizures without neurologic deficit, and this patient did *not* have neurologic deficit. It was for that reason we did first an arteriogram to rule out the possibility of a vascular anomaly. An arteriovenous malformation diffused over the temporal parietal frontal lobe would provide a beautiful explanation fitting the entire situation.

On the basis of the arteriogram, showing high arterial elevation above the temporal lobe, we felt the patient had a tumor, mainly in the temporal lobe of the brain. Because of the size of the tumor and because of the absence of neurologic signs, we thought it might be one of two things which would *not* be fatal.

A meningioma can diffuse without producing much neurologic deficit, and meningioma of the sphenoidal ridge can produce this identical clinical picture. Sphenoid ridge meningioma was one favorable thing the patient could have had. Secondly, the large elevation and sort of curve in the x-ray makes you think it might be a big cyst. An astrocytoma can be cystic, and a cystic astrocytoma can be favorably attacked.

Those were the two favorable lesions that he could have had. The unfavorable lesion was any type of infiltrating glioma in this location—unfavorable because this is the dominant hemisphere, near the motor, speech, auditory, sensory and other important areas. So we felt, after arteriograms, confirmed by ventriculogram, that the patient had a lesion in this region which we hoped was cystic astrocytoma or meningioma. If it was not, then we had fundamentally a problem as to whether it was glioblastoma, astrocytoma, or oligodendroglioma. One cannot excise the motor-sensory area and have anything worthwhile left.

We sometimes like to do biopsies before craniotomy, and, in cases that prove inoperable, we spare the patient a craniotomy. The location involved here is one in which needle biopsy is *not* feasible because one has to start blindly needling through important tissues in the speech area. We don't like to needle several times, missing the tumor, finally hitting an operable tumor but having rendered the patient aphasic by this blind needling. So this is one case where we felt it was all or nothing—to turn a flap and hope to find an astrocytoma that was cystic, or a meningioma. If it was glioma, fundamentally the thing would be inoperable. So it proved.

At surgery, we found *no* sphenoid ridge meningioma, we found *no* cyst. There was a large, solid, infiltrating astrocytoma (which the student correctly deduced) through the central lobe. The pathologist will tell you of its extension. But, fundamentally, it was an infiltrating glioma in the dominant hemisphere. It's amazing that the patient didn't have neurologic signs. He should have been aphasic, hemiphlegic and hemianoptic, but he wasn't.

When the neurosurgeon faces an inoperable tumor, we just have to say we're stuck. The best we could do here was *not* a total removal, rendering the patient amnesic and aphasic. We don't purposely do that. We thus were limited to what solid brain we could remove in the left temporal lobe. We know from the work that's done for vasomotor epilepsy and frontal lobectomies that one can remove about five centimeters from the tip of either temporal lobe without creating neurologic deficit. It is below the motor speech area, anterior to the visual pathway, and so we took just that much of the brain and amputated the left temporal horn. There, I think, is the reason for the patient's death. Had we grossly removed the entire temporal lobe and tumor, the surgery would not have been fatal; as it was, an inadequate internal decompression left the area filled with a large brain tumor.

Figure 1. Arteriogram, showing displacement of vessels farther from base than is normal.

We did *not* create neurologic deficit with our surgery because it was done under local anesthesia. Purposely, it was done under local anesthesia so we could have the patient talking and moving the right side as we worked, to be sure we weren't taking too much. At the end of surgery the patient responded nicely, had *no* hemiplegia, *no* aphasia, *no* hemianopsia—came out of it in fine shape.

But then came that serious train of events that follows intracranial surgery if you have failed to remove the tumor. It was then that he got into dire straits from a situation which, I think, was the inevitable cause of his death.

Dr. Leland D. Stoddard (Pathology): Dr. Williamson, can you tell us a little about the hemorrhage into the area of the tumor that we are going to see in the gross. Do you think that it came on after the operation, during it, or immediately afterward?

Dr. Williamson: There was *no* dire trouble with the tumor at the time of surgery. We were faced, of course, with the postoperative decision when the patient became critical: Was there postoperative hemorrhage? In such a case we could raise the flap and evacuate it. The pathologist will always find, when surgery is unsuccessful after craniotomy, some blood in the tumor bed. These patients don't die unless a great big clot compresses vital areas.

PATHOLOGY REPORT

Dr. J. David Robertson (Pathology and Oncology): A large, diffusely infiltrating tumor occupied the left frontal, parietal, and temporal lobes, as you will see in these coronal sections of the brain.

The first section showing tumor was taken about four centimeters from the frontal poles. In most areas the tumor was white, firm, and solid; but in one area there were numerous small cysts. A section farther posterior revealed the surgical removal of the temporal pole and postoperative hemorrhage within the tumor occupying the parietal lobe. The tumor involved the lenticular nuclei but did not extend into the internal capsule, which lies deep to these structures. You can easily see that the expand-

ing mass of the tumor had pushed the midline to the right.

Along the medial aspect of the occipital lobes there were areas of fresh hemorrhagic necrosis that followed the convolutional contours. Likewise, in the pons, principally on the right side, there were multiple hemorrhages.

Dr. Stoddard: As you have seen, this large tumor produced changes in several different ways. One way was by actually infiltrating important areas. Another way was by compressing contiguous areas of the brain. For example, the motor area was compressed as much as it was infiltrated. Still another way that the tumor produced changes was simply by increasing the mass of the brain. Therefore, the left side was pushed to the right. Not only that, but the mass pushed downward, and the hippocampal gyrus was pressed against the tentorium. In turn, the tentorium was pressed upon the posterior cerebral arteries, which serve the occipital poles and also the pons. Hence, there were foci of necrosis and hemorrhage bilaterally in the distribution of the posterior cerebral arteries.

Histologically, the tumor was an astrocytoma.

The tumor greatly expanded this gyrus as it infiltrated it and compressed the adjacent gyrus. That is rather characteristic of astrocytomas.

Next, I want to show you how an astrocytoma involves more and more of the brain. This type of glioma is almost never well demarcated from surrounding brain. Here you see a more or less nebulous transitional area in which some neurones remained amidst the proliferating astrocytes.

We are talking now about the solid astrocytoma, the common type of astrocytoma arising in the cerebral hemispheres of adults. Although you have already seen some small cystic spaces in this tumor, it was not at all like the cystic cerebellar astrocytoma, which has one very large cyst and a tumor nodule in its wall.

I want to mention again the distant effects of this tumor—the results of compression of the posterior cerebral arteries. Here a pontine branch is seen in this histological section. The first result of vascular injury probably was edema. Then, with further injury, there was hemorrhage, necrosis of parenchyma, and a consequent polymorphonuclear leukocytic exudate infiltrating the walls of the vessel.

What happened to the patient terminally? There was postoperative hemorrhage in the tumor. The brain also was somewhat swollen. Both contributed to increasing intracranial pressure. Then, the patient had been complaining of pain in the abdomen. Perhaps the pain was related to gastromalacia, which may occur in cases of cerebral lesions of various sorts. There were hemorrhages in the stomach, and perhaps these lesions were developing during the last week. The fever was no doubt the consequence of terminal bronchopneumonia.

There were a few incidental findings. The calcifications mentioned by Dr. Tice were stones in the upper pole of the right kidney. Other lesions are listed in the diagnosis.

ANATOMICAL DIAGNOSIS

Primary:

Astrocytoma of the left frontal, parietal and temporal lobes causing shift of the brain to the right and bilateral tentorial compression of the posterior cerebral arteries.

Bilateral focal necroses and hemorrhages in occipital lobes and in pons.

Operative wound, left temporal region. (History of craniotomy and partial removal of left temporal lobe three days before death.)

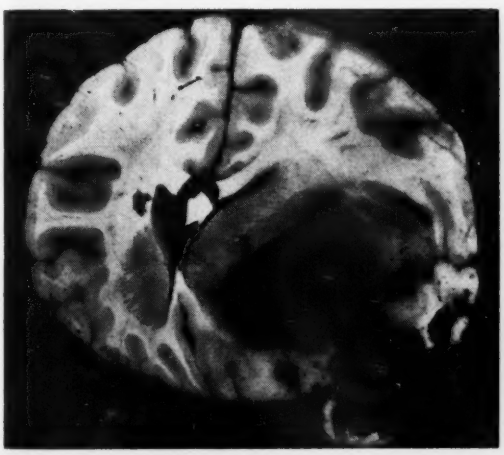

Figure 2. Coronal section of the brain viewed from front to back. The poorly defined tumor mass occupies the left basal nuclei, internal capsule, and cortex of the temporal and parietal lobes; compresses the left lateral ventricle; and shifts the midline to the opposite side. Post-operative hemorrhage within main tumor mass and adjoining temporal lobe. Infiltrating tumor enlarges lower convolutions and obscures pattern of gray and white matter.

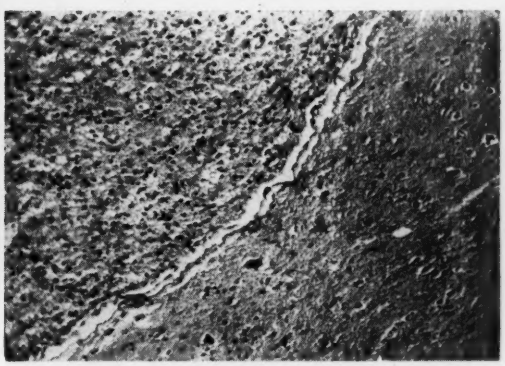

Figure 3. Photomicrograph of astrocytoma involving convolution to the left and above. The sulcus separates this convolution from adjoining convolution uninvolved by the tumor.

Trephine wounds, occipital lobes, bilateral. (History of ventriculogram three days before death.)
Drainage wound, right occipital area.
Gastromalacia and focal gastric and duodenal hemorrhages.
Terminal bronchopneumonia, bilateral.
Acute splenic tumor.
Paracentral hepatic necrosis.

Accessory:

Cystitis, minimal.
Chronic pyelonephritis and nephrolithiasis, upper pole, right kidney.
Arteriosclerosis, aorta, slight.
Fibrous pleural adhesions, left lower lobe.

SUMMARY

The patient with convulsive seizures always presents a problem of challenge and great responsibility to the physician. The responsibility is that of making an accurate and complete diagnosis; otherwise therapy may long be misdirected. This is well illustrated in the case here discussed.

Licenses to 49 Physicians

A list of 49 physicians, newly licensed to practice medicine in Kansas, was released recently by the Kansas State Board of Medical Registration and Examination. Included were 41 who were licensed by endorsement and eight who successfully passed examinations given December 10 and 11, 1952.

The names and addresses of those licensed by endorsement are as follows: Walter Eugene Blevins, Hugoton; Bernard Stephen Brody, Topeka; David James Buddrus, Mission; LeGrand B. Byington, Kansas City, Missouri; Clair Joseph Cavanaugh, Great Bend; Edwin Harold Church, Topeka; Kendall Allen Clark, Atlanta, Georgia; James Atwood Dugger, Topeka; Ronald Joseph Garst, Satanta; Joseph Gendel, Topeka; Thomas Warne Graham, Leavenworth; George Henry Hanlon, Gouverneur, New York; Jack Edward Hilgers, Plainville; James Cotter Hirschberg, Topeka; Clifford William Hogan, Jamestown, North Dakota; Gilbert Frederick Jordan, Wichita.

Betsy Anne Ledbetter, Manhattan; Edward Sharpe Lee, Jr., Portsmouth, Virginia; Joseph Gibson Lockhart, Philadelphia; Francis Nick Lohrenz, Kansas City; Harold Ray Lyddon, Jr., Kansas City, Missouri; Alice Marsh, Kansas City; Dean McCandless, St. John; Duncan Alex McLauchlan, Wichita; Lunetta Anna Memming, Lawrence; Donald Charles Niederluecke, Valley Falls; Richard Lee Owens, Kansas City, Missouri; Irving Philips, Topeka; John Robert Rufe, Kansas City, Missouri.

Bettye Sue C. Schurter, Hardtner; Lonis Leon Schurter, Hardtner; John Darrell Smith, Hugoton; Henry Bernard Stryker, Concordia; Julius Austen Tabris, Kansas City, Missouri; James Alvin Taylor, Parsons; Jane Wasson Tillinghast, Kansas City; Girard Veenschoten, Jetmore; Thomas Aloysius Weldon, Perry; Daniel Coyle Wilkerson, Leavenworth; Lawrence Edward Woodard, Wichita, and Ruth Ethel Wright, Sedan.

Those who were licensed by examination were Henry Joseph Biermann, Wichita; Chauncey Goodrich Bly, Kansas City; Murray Morris Cash, Tulsa; William LeRoy Doane, Kansas City, Missouri; Harry Tsuneo Hidaka, Wichita; Gilbert Francis Norwood, Kansas City; George Gayle Stephens, Wichita, and Willard Fisher Werner, Denver.

Nominations for 1953

Officers of the Kansas Medical Society for the year beginning on May 7, 1953, will be elected by the House of Delegates at its meeting on that day. Ballots will show the names of those listed below, as selected by the Nominating Committee at its meeting on January 20, and additional nominations may be made from the floor. Those now holding offices are indicated by asterisks.

President-elect	*Murray C. Eddy, M.D., Hays
	Thomas P. Butcher, M.D., Emporia
First Vice President	*John M. Porter, M.D., Concordia
	Karl E. Voldeng, M.D., Wellington
Second Vice President	Clyde W. Miller, M.D., Wichita
	Frederick E. Wrightman, M.D., Sabetha
Constitutional Secretary	*Dale D. Vermillion, M.D., Goodland
	Albert C. Armitage, M.D., Hutchinson
Treasurer	*John L. Lattimore, M.D., Topeka
	Dwight Lawson, M.D., Topeka
AMA Delegate	George F. Gsell, M.D., Wichita
	Cyril V. Black, M.D., Pratt
AMA Alternate	*Peter E. Hiebert, M.D., Kansas City
	Lee H. Leger, M.D., Kansas City

Fewer Applicants for Medical Schools

Continuing a three-year trend, the number of students applying for admission to the nation's medical schools declined again this year, according to the official study of 1952-1953 applicants by the Association of American Medical Colleges.

Some 3,150 fewer persons applied this year than in the 1951-1952 year, and some 7,600 less than three years ago. This means that competition among the medical schools for high-ranking students is increasing. Of 16,763 persons who made application last fall, 7,778 were accepted.

The survey shows that the average pre-medical student applies to three or four medical schools, so that no school can expect to have every student it selects.

A physician who mentions a company's advertisement in the Journal to that company's representative shows his appreciation for the support given this publication.

ACTIVITIES OF MEMBERS

Dr. William J. Reals has returned from duty with the armed forces and is now pathologist at St. Joseph Hospital, Wichita.

Dr. Mary T. D. Glassen, Phillipsburg, has announced that Dr. Barbara Calderwood, who will complete her internship at Menorah Hospital, Kansas City, in June, will then be associated with her in practice at the Phillipsburg Health Center. Dr. Calderwood took her preceptorship under Dr. Glassen while attending the University of Kansas School of Medicine.

Dr. Ernest D. Erickson, who joined the staff of the Arkansas City Medical and Surgical Clinic last July, has been called to active duty with the Army. He is reporting to San Antonio this month for two months at a medical field service school prior to reassignment.

Dr. O'Ruth Petterson, Wichita, discussed "Infectious Diseases of Childhood" before the Alcott School Parent-Teachers Association recently.

Dr. Homer B. Russell, Great Bend, has gone to Chicago for a year's postgraduate work at St. Luke's Hospital. Before leaving he resigned appointments as city and Barton County health officer.

Dr. Rowe F. Bisbee, formerly obstetrician and gynecologist at the Sugg Clinic, Ada, Oklahoma, has opened an office in Salina. He is a graduate of Washington University School of Medicine, St. Louis, and has had two years' service with the medical corps of the Army in the South Pacific and the Far East.

Dr. E. R. Beiderwell, Garden City, opened an office in Leoti in February at the time of the opening of the new public hospital there.

Dr. John C. Artman, who has been associated in practice with Dr. William Brewer and Dr. Lloyd W. Reynolds in Hays during the past two and one-half years, has been recalled to active service in the Navy. He plans to return to Hays on completion of his tour of duty.

Dr. Robert L. McAllister, Marysville, was recently named health officer for Marshall County, succeeding the late Dr. O. P. Wood.

Dr. Herbert L. Bunker, Jr., who recently returned from military service to his home in Junction City, is now associated in practice there with Dr. F. W. O'Donnell, Dr. A. E. O'Donnell and Dr. Harry O'Donnell.

Dr. Donald Niederluecke, who was graduated from the University of Nebraska School of Medicine in 1951, has opened an office for practice in Valley Falls.

Dr. Fred A. Garvin, who has practiced in Augusta for more than 50 years, was guest of honor at a community celebration on February 4, with the Augusta Chamber of Commerce as host. Dr. Edward H. Hashinger, of the University of Kansas School of Medicine, was guest speaker on the program following a dinner.

Dr. Karl Menninger, director of education for the Menninger Foundation, Topeka, received the annual citation of the Topeka Chapter of the National Conference of Christians and Jews at a dinner held on February 19. He was recognized as "a Topekan who has contributed notably to the cause of world brotherhood."

Dr. Thomas Aloysius Weldon has opened an office in Perry. He was graduated from the Stritch School of Medicine of Loyola University, Chicago, in 1950.

Dr. Howard E. Snyder, Winfield, will preside at a symposium on cancer to be held in connection with a sectional meeting of the American College of Surgeons in Oklahoma City, March 24 and 25.

Dr. William S. Swart and Dr. Lindley E. Strode, Girard, were presented 50-year membership pins at a recent meeting of the Girard Blue Lodge.

Motion Picture Reviews Available

The fourth supplement to the booklet entitled "Reviews of Medical Motion Pictures" was published recently by the Committee on Medical Motion Pictures of the A.M.A. Copies may be requested from the committee, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

COUNTY SOCIETIES

Dr. Orval L. Smith, St. Marys, was elected president of the Pottawatomie County Medical Society at a meeting held last month. Dr. Edward Goldsich, St. Marys, was named secretary.

A recent meeting of the Miami County Society, held at the state hospital at Osawatomie, was attended by physicians from Miami, Anderson, Franklin and Johnson counties. Dr. Charles C. Dennie, Kansas City, was guest speaker. His subject was "Unusual Reactions to Antibiotics."

Dr. J. Howard Gilbert, Seneca, was elected president of the Nemaha County Society at a meeting held in Sabetha recently. Dr. Thomas A. Montgomery, Sabetha, was elected vice president, and Dr. Martin J. Rucker, Sabetha, secretary.

As part of the observance of the Sedgwick County Medical Society's 50th anniversary, the group is sponsoring a series of three medical meetings open to the public. The first, held on February 12, featured a talk on heart disease by Dr. R. W. Wilkins of Boston. Speaker for the second meeting, on March 3, will be Dr. Melvin Casberg, chairman of the Armed Forces Policy Committee for the National Blood Program. The final meeting, on April 1, will introduce Dr. C. P. Rhoads, New York, who will speak on advancements in treatment of cancer.

Mr. Roy Johnson, director of the Hospital Facilities Division, Kansas State Board of Health, was guest speaker at the January meeting of the Montgomery County Society. He discussed hospital construction in Kansas, mentioning that 70 new hospitals have been put into operation in the last six years.

The February meeting of the Shawnee County Society was held at the group's new building, 315 West Fourth Street, Topeka, on February 2. Dr. Alfred R. Sugg, Ada, Oklahoma, spoke on "Prostatism." The following physicians were elected to membership: Dr. J. Cotter Hirschberg and Dr. Prescott W. Thompson, Menninger Foundation; Dr. Joseph Gendel, orthopedist, Topeka Medical Center; Dr. G. Bernard Joyce, orthopedist practicing in partnership with Dr. Clyde B. Trees. Two physicians were elected to emeritus membership, Dr. G. L. Kerley and Dr. J. F. Northrup.

A joint meeting of members of the Sedgwick County Society and pharmacists of Wichita was held at the Allis Hotel, Wichita, on February 3. Mr. Sam Alfind, chief of the Kansas City Division of the Pure Food and Drug Administration, was guest speaker.

Members of the Allen County Medical Society were guests of the Allen County Medical Assistants' Society at a dinner meeting in Iola on February 10. Dr. Warren F. Bernstorf, Winfield, president of the Kansas Medical Society, was guest speaker.

Advertisers appreciate the patronage of Journal readers. All products advertised carry the seal of acceptance of the various councils of the A.M.A.

DEATH NOTICES

Edgar C. Duncan, M.D.

Dr. E. C. Duncan, 77, who served as president of the Kansas Medical Society in 1931, died at his home in Fredonia on February 12. He had practiced there since his graduation from Beaumont Medical College and Hospital, St. Louis, in 1901.

Soon after war was declared in April, 1917, Dr. Duncan organized a Red Cross ambulance company for service in France, and the unit was later taken into the Army with Dr. Duncan as commanding officer. The company served overseas for a year, after which Dr. Duncan remained active in the reserve and became colonel commanding the medical regiment of the 89th division reserve.

He was active in his local medical society, having been an officer for many years, and was interested in civic affairs also. He had served as mayor of Fredonia and as president of the city's chamber of commerce.

Alfred E. Gardner, M.D.

Dr. A. E. Gardner, 83, who practiced medicine in Wichita 40 years before his retirement in 1948, died on February 9 in a Wichita hospital. He was an honorary member of the Sedgwick County Medical Society.

Dr. Gardner was graduated from the University of Louisville School of Medicine in 1895, and practiced for 10 years in Kentucky in Morgantown and Louisville. He then moved to Kansas and remained here except for a period during World War I when he served as a major in the medical corps. He was a fellow of the American College of Surgeons.

BLUE SHIELD

Professional Relations

At a recent conference in Chicago attended by representatives from the Departments of Professional Relations of Blue Cross-Blue Shield Plans from all over the United States, and some from Canada, it was most interesting to note the difference in concepts, attitudes, and techniques. These three subjects were suggested as a theme for workshop discussion during the conference, and were explored thoroughly.

In one group the concept finally approved was that Blue Cross and Blue Shield are non-profit community instruments of hospitals and physicians for making their services available to the American people through voluntary prepayment. This concept was agreed upon after much discussion. Many plans seem to be afraid to use certain terms because of the wrong connotation which might be given them. It was evident that the plans serving large industrial areas have an entirely different approach to a problem which is also different in many aspects. The highly industrialized areas must compete on a different level and must always bear in mind the kind of groups they are serving.

Attitudes toward the plans and toward the physician and hospital relationships seem to be governed also by geographical differences. The almost complete co-operation which now exists between physicians, hospitals, and the plans in the so-called rural states seems to be a desirable result which has not been achieved in many other areas. In some places where there is a division between the two plans, hospital calls are never made by anyone representing the Department of Physician Relations and vice versa. This seems a most unhappy situation, and it is hoped such differences of opinion will never become important in the relationships between physicians, hospitals, and the plans.

In describing the techniques used in the Kansas plan, the development of State Member Councils was unique among all other plans. The Kansas delegation told the group how it is being developed in Kansas and with what success in cementing existing relationships between members and the plan and forming new relationships. This seems to be a new idea in Blue Cross-Blue Shield relations, and Kansas is apparently leading in its development.

It has been deemed such an important program in Kansas that a new director has been brought into the office to set up member councils at three different levels, first in the community, second in the district, and third state-wide. These will be groups of interested members of Blue Cross and Blue Shield who are eager to assist the hospitals and the doctors in administering a program which will benefit all and which can be maintained at the lowest cost possible. George Beverly, one of the representatives who has been working in the Garden City area, has been selected to direct this program.

A very homely comparison was used which bears repeating. The whole program was likened to a three-legged milk stool, one leg of which would be physicians, another leg hospitals, the third leg the Blue Cross-Blue Shield plans. Complete coordination between the three legs must necessarily be maintained. In finer words, a triad has been formed which should result in the lowest possible cost for the highest possible standard of physician and hospital care.

Activities of Radiological Society

A joint meeting of the Kansas Radiological Society and the Radiological Society of Greater Kansas City was held at the University of Kansas Medical Center, Kansas City, February 16, 17, and 18. In cooperation with these organizations, the Kansas Medical Society, the Kansas State Board of Health, and the University of Kansas School of Medicine presented a postgraduate course in radiology.

Dr. Anthony Rossitto, Wichita, was elected president of the Kansas Radiological Society at a dinner session held at the Terrace Club the evening of the 16th. Dr. A. M. Cherner, Hays, was named vice president, and Dr. Willis L. Beller, Topeka, was chosen as secretary-treasurer. It was announced that the society had been awarded a certificate of merit for its exhibits at the Kansas City Southwest Clinical Society meeting in 1952. The society voted to donate $50 in prizes for a contest to be sponsored by the Kansas Society of X-ray Technicians in Kansas City in March, 1953.

The following Kansas radiologists presented papers at the postgraduate course: Dr. Lewis G. Allen, Kansas City; Dr. Beller; Dr. Allan K. Briney, Topeka; Dr. Cherner; Dr. Leland F. Glaser, Hutchinson; Dr. Homer L. Hiebert, Topeka; Dr. Ralph P. Hines, Wichita; Dr. John R. Kline, Wichita; Dr. Doris A. Kubin, Kansas City; Dr. Hans Lewin, Topeka; Dr. Warren S. Peiper, Arkansas City; Dr. Rossitto; Dr. James R. Stark, Wichita; Dr Galen M. Tice, Kansas City, and Dr. Charles M. White, Wichita.

Prominent guest speakers included Dr. Simeon T. Cantril, Seattle; Dr. Isadore Lamp, Ann Arbor; Dr. Isadore Meschan, Little Rock; Dr. Edward B. D. Neuhauser, Boston, and Dr. David G. Pugh, Mayo Clinic, Rochester.

A meeting of the Kansas Radiological Society will be held in Wichita in early May, at the time of the annual session of the Kansas Medical Society.

Present Status of the Hormonal Therapy of Cancer of the Breast and Prostate*

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INTRODUCTION

The relationship of the steroid hormones of the body to the growth or to the inhibition of growth of certain neoplasms has been known for many years. Hormonal therapy has proved effective for at least five types of neoplastic disease. There are malignant lesions of the: (1) breast (both male and female), (2) prostate gland, (3) uterus, (4) lymphatics system and (5) hematopoietic system.

Through intense research in the past 12 years, hormones have come out of the experimental laboratory and are now being used routinely by the clinician as one of the few effective tools in the campaign against malignancy. However, experience by experts in this field has shown conclusively that while steroid hormones are effective in some cases, there still may often follow complete failure or, more important still, undesirable side reactions. In other instances, malignancy in another part of the body may be initiated.

Thus, it should be stated clearly at the beginning that indiscriminate therapy of cancer with steroid hormones by one improperly trained or uninformed, may cause more harm than good. The general practitioner should have knowledge of what type of hormonal therapy can be used for patients with malignancy. It is the purpose of this paper to present as far as possible the most up-to-date management of neoplasms by the use of steroid hormone therapy and related surgical procedures. While no attempt has been made to review every article written on the subject, an attempt is made at reviewing some of the more important ones.

MALIGNANT LESIONS OF THE FEMALE BREAST

The exact role of estrogens as etiologic agents in female breast carcinoma is still obscure. Nathanson[1] concludes that "excretion studies of the hormones with the present methods have failed to yield much information." He further states, "there is no significant deviation in the excretion of sex hormones in women with breast cancer; there is no proof that sex hormones are not involved in the disease or that abnormal secretion of the hormones does not accompany or precede the development of breast cancer. It is significant that normal excretion rates may be found in the presence of breast cancer; and cancer of the breast may be independent of hormonal influence once it develops. Definite proof for the hormones as the direct cause of cancer is lacking."

It is an interesting finding, also by Nathanson,[1] that there is a higher incidence of carcinoma of the breast in women who have not borne children than in those women who have. Twombley[2] has introduced the interesting theory that regression of breast cancer may occur with a change in the hormone balance within the patient's body.

Use of Estrogens: Haddow[3, 4] in England and later Nathanson[1] in the United States showed that estrogens could be helpful in mammary carcinoma, and they have reported satisfactory regression of metastatic lesions. In other cases they have been able to demonstrate spectacular healing of the primary tumor. Nathanson[1] in his early reports stated that "favorable results occur in women past the menopause, whereas estrogens in younger women with breast cancer seem apt to stimulate rather than depress the growth rate." As pointed out by McCullagh,[5] this would seem paradoxical in light of the fact that "the rate of growth of malignant breast tissue should be decelerated by substances which at one time accelerated the development of the same tissue." However, such facts are now firmly established.[6]

The most valuable single factor in estrogen therapy is impressive symptomatic relief of pain. Adair[7] has reported that his patients were symptomatically improved in spite of the fact that the disease was progressive. He also has shown that distant metastases respond favorably with estrogen therapy in the skin, lymph nodes, pleurae, and in some instances in the primary tumor itself. He was unable to obtain symptomatic relief from pain in osseous metastases; however, Garland, Baker, Picard and Sisson[8] have reported that from 40 to 70 per cent of patients with osseous metastases from breast cancer are relieved of pain by steroid hormone therapy. They state that the average survival time of patients treated with steroid hormones is 8.8 months. Cutler, Schlemenson, Kearney, and Caceres[9] observed that "palliation occurred most frequently in patients over 60 years.

* This is one of 11 senior theses selected for publication by the Editorial Board from a group of 15 judged the best by the faculty of the University of Kansas School of Medicine.

The effects were noted in both bone and soft tissue metastases." It is their opinion that "certain patients with advanced carcinoma of the breast experience relief from pain and a sense of well-being during estrogen therapy, even in the absence of objective improvement."

Suffice it to say that estrogens are of value in the palliative treatment of mammary carcinoma, but should not replace surgery as the primary treatment. They have a valuable supportive role in relieving pain, improving health, and prolonging life in some patients.

Drugs and Dosage: The drugs utilized in the treatment of breast carcinoma are as follows: diethylstilbestrol, 15 mg. daily; ethinyl estradiol, 3 mg. daily; Premarin, 30 mg. daily; estradiol dipropionate, 5 mg. twice weekly (IM); dienestrol, 15 mg. daily; dimethyl ether of diethylstilbestrol, 30 mg. daily; and tri-para-anisyl-chloroethylene (TACE), 24 mg. daily.

Diethylstilbestrol is probably the hormone of choice and the one most widely used today. The hormone is used by some for three to six months, duration varying with the age of the patient and the occurrence of various side effects.

Untoward Side Effects: Some of the more striking side effects are nausea, vomiting, tender breasts and nipples, especially in younger women, increase in pigmentation, incontinence of urinary bladder, and vaginal bleeding. However, the chief danger in estrogen therapy is to be found in an acceleration of malignant growth in younger women. For this reason, the 1950 report of the American Medical Association Council on Pharmacy and Chemistry[10] (see below), advises that "any patient who still menstruates or who has menstruated within five years should definitely not receive estrogen therapy as it accelerates the rate of growth of the carcinoma. In no case should estrogen therapy replace radical surgery in treatment of breast carcinoma."

Castration: The subject of castration is too lengthy to be dealt with fully here. However, it should be remembered as an indirect method of "hormone" therapy. Two methods should be considered: (1) prophylactic and (2) therapeutic castration. The purpose of both is to reduce internal secretion of estrogens. The rationale of these methods is based upon the findings of such workers as Harrell,[11] who showed conclusively that malignancy of the breast was ten times greater in normal women than in castrated females, and that castration early in life was an important factor. Two methods have been used in castration. One is surgery and the other is x-radiation. Because of the uncertainty of the latter method in obtaining complete castration, Nathanson and Kelley[12] are of the opinion that "there has been a trend toward ovariectomy in young women when their condition permits it, reserving radiation for women over 40, when ovarian action is beginning to wane."

Use of Androgens: The rationale of the use of androgens in mammary carcinoma is their action to inhibit or neutralize the effect of estrogens within the body. Androgens like estrogens have proved to be only palliative, not curative, in mammary cancer. It has been the opinion of McCullagh[5] that androgens are more effective than estrogens and have their greatest value in advanced cases of breast malignancy with metastases to the bone and lung. "Unfortunately," he states, "in some patients the entire disease appears to take on increased vigor during therapy." The latter was essentially the finding of Farrow and Woodard[13] who, in 1940, first began treating mammary carcinoma with injections of testosterone propionate. They concluded at that time that "testosterone in large doses exerts a stimulating rather than an inhibiting effect on growth of metastatic mammary carcinoma."

In 1946, Adair and Hermann[14] found that large doses of testosterone (50 to 200 mg. two to three times per week) gave striking improvement in four of eleven patients treated and in three bone metastases recalcified; also, in one patient it was felt that there was temporary regression of an extensive primary tumor.

Twombley[2] reported that "twenty-eight per cent of bone metastases from carcinoma of the breast will respond to testosterone therapy, at least temporarily." The reports of Farrow and Woodard[13] and those of Huggins[15] have stressed the caution that must be used with testosterone therapy, because of the danger of stimulation rather than inhibition of malignant growth. Huggins [15] also believes that testosterone is "most beneficial in giving temporary relief in patients with osseous metastases." However, he also calls attention to the fact that certain undesirable side effects may offset any good results.

It has been an interesting speculation that testosterone therapy might be used with castration following mastectomy in an attempt to limit the growth of distant metastases. However, results have been discouraging and, as Snapper[16] has pointed out, "Castration and testosterone treatment does not offer an effective protection against the formation of metastases in patients who have been operated on for carcinoma of the breast with axillary involvement." With this combined method it was hoped that it might be of value in (1) causing regression of metastases following mastectomy and (2) as a precaution against recurrence following mastectomy without metastases. However, results are poor and in many cases recurrence has occurred in spite of any choice of therapy.

In 1941, Lowser[17] found favorable changes in patients with advanced mammary carcinoma by the use

of testosterone propionate. Farrow and Woodard,[18] on the other hand, found that the use of small doses of testosterone in some cases caused accelerated growth of osseous metastases. They further reported that "testosterone is contraindicated in patients with hypercalcemia associated with osseous metastases." They warned that "routine blood chemical studies in patients receiving testosterone therapy is obvious." They cite one case in which "the androgen at first appeared to activate the lesions and later to inactivate them." They concluded, "it would appear that in many instances a favorable status may be maintained until pulmonary or liver metastasis appears." They further state that "when this occurs the patient rapidly retrogresses and dies within a relatively short time despite the continued administration of the androgen." These findings were again supported by Adair in 1949.[18] Preston, Taylor, and Crumrine[19] have reported satisfactory regression of bony metastases with decalcification of osteoplastic metastases and recalcification of osteolytic metastases.

Drugs and Dosages: Testosterone propionate is by far the most commonly used androgen. However, Nathanson and Kelley[12] state that crystalline suspensions of testosterone, methyl testosterone, and testosterone cyclopentyl propionate "appear to be as effective as testosterone propionate when given in comparable dosages."

The usual dosages used range from 150 to 300 mg. weekly in at least three divided doses; however, larger doses (100 to 200 mg. daily) have been recommended. Huggins[15] suggests that testosterone propionate should be given in 25 mg. doses intramuscularly daily. Nathanson[20] suggests 50 to 100 mg. intramuscularly three times weekly. Garland, Baker, Picard, and Sisson[8] are of the opinion that "there is no consistent difference in the favorable results between low dosage rate (e.g., 75 mg. per week) and high dosage rates (600 mg. per week) when treatment is continued for at least two months.

Undesirable Side Effects: Huggins[15] has stated that the most common and significant side effects in the female are masculinization, hypercalcemia, and heart failure. Adair and Hermann[14] have pointed out that "it would appear that testosterone is contraindicated in patients with hypercalcemia associated with osseous metastases. The importance of routine blood chemical studies in patients receiving testosterone therapy is obvious." Adair[7] reports in his experience "the more noticeable side effects after the administration of androgens were increase in weight, edema of the lower extremities, deepened voice, hirsutism, and acne."

Remarks: For a more adequate summary of the present trend of thought regarding the subjects considered above, the recommendations of the Subcommittee on Steroids and Cancer, Committee on Research of the American Medical Association, Council on Pharmacy and Chemistry, in their 1951 report, have best presented the conclusions to be drawn from research and clinical experience up until the present date. They are as follows:[10]

1. The best curative measure for mammary carcinoma available at present is early diagnosis and radical surgical removal of the tumor and surrounding tissue.

2. Three palliative measures are available to deal with metastatic mammary cancer: surgery for localized lesions, irradiation and hormone therapy. For most osseous or soft tissue lesions, irradiation is the treatment of choice; lung lesions and very widespread osseous or soft tissue metastases may best be treated with hormone therapy.

3. The response of lesions to testosterone propionate does not appear to depend particularly on the physiologic age of the patient, whereas, estrogen therapy is ineffective and dangerous in premenopausal patients or patients at the menopause. The effectiveness of estrogen therapy of soft tissue and lung metastases appears to increase with the age of the patient.

4. Testosterone propionate is the hormone of choice for treatment of premenopausal women regardless of site of lesions. However, it should be remembered that castration is usually more effective in the premenopausal woman, and this should be the treatment of choice if there are no contraindications. In women five years or more postmenopausal, estrogens are the hormones of choice for treatment of soft tissue and lung metastases. Although osseous lesions of postmenopausal women respond equally to testosterone propionate or to estrogens, the superiority of testosterone in controlling subjective symptoms, particularly pain, makes it appear to be the drug of choice for these metastases.

5. The location of bone metastases does not influence the response. Skin and lymph node lesions respond more frequently than do other soft tissue lesions. Abdominal metastases are reported to respond least often.

6. An effective dosage schedule of testosterone propionate appears to be 50 mg. given three times weekly. The minimum total dose is about 3 Gm., and the minimum length of therapy should be three months before concluding that a patient will not respond.

7. The minimum total dose of diethylstilbestrol, dienestrol, Premarin, and the dimethyl ether of diethylstilbestrol appears to be about 4 Gm. and the minimum duration of therapy about three to six months. For ethinyl estradiol and estradiol dipropionate, the minimum total dose appears to be 200 mg. and the minimum duration of therapy three to six months.

8. For the present, it is suggested that treatment

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Hechter, Dopkeen and Yudell[1] have found that the use of hyaluronidase has "markedly increased the rates of absorption and administration of hypodermoclysis with no untoward reactions." They also found that extremely small amounts of this enzyme facilitated the absorption of fluids in that greater amounts of fluids were absorbed by the patient in a given period of time and that the localized swelling following hypodermoclysis disappeared more promptly.

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1. Hechter, O.; Dopkeen, S. K., and Yudell, M. H.: The Clinical Use of Hyaluronidase in Hypodermoclysis, J. Pediat. 30:645 (June) 1947.
2. Schwartzman, J.; Henderson, A. T., and King, W. E.: Hyaluronidase in Fluid Administration: A Preliminary Report, J. Pediat. 33:267 (Sept.) 1948.

with hormones should be continued until reactivation or steady progression of the disease occurs. Cessation of therapy after reactivation may result in another regression. Change of therapy to another hormone may also bring about a second favorable response.

9. The mean duration of improvement of soft tissue lesions, treated either with testosterone or estrogen, is about 10 to 12 months; for bony lesions testosterone will produce a mean duration of improvement of about 11 to 12 months, whereas the mean duration of improvement with estrogen is 16 to 18 months.

10. The mean survival time after admission to this study of all patients who have died is 8.5 months for testosterone-treated patients and 9.8 months for estrogen-treated patients. Patients who showed improvement survived about twice as long as those who did not show improvement.

11. Both testosterone propionate and the estrogens, in these doses, produce unpleasant side effects in a high proportion of patients. Two side effects, edema and hypercalcemia, are dangerous and require constant observation of the patient and early corrective measures. Estrogen therapy may cause severe uterine bleeding requiring curettage. With prolonged bleeding, the possibility of endometrial carcinoma or activation of fibroids must be considered.

12. Histologic examination of biopsy and autopsy material collected in this study has not revealed any changes in tumor cells or stroma which would suggest an explanation of the mechanism of hormonal action in metastatic breast cancer. At times, however, there was complete disappearance of tumor in satellite skin nodules, in focal areas within the breast carcinoma, and in occasional lymph nodes previously replaced by tumor. The changes seen both in the tumor and stromal background in the cases responding to steroid therapy are comparable to the effects of irradiation.

MALIGNANT LESIONS OF THE MALE BREAST

Carcinoma of the male breast is not common. In fact, as of 1951, Campbell and Cummins[21] reported that only 13 well authenticated cases were on record. These were all associated with estrogenic therapy for prostatic carcinoma in the male. Regarding the question of etiology, they have stressed the point that "if estrogens are carcinogenic to the human male breasts, the occurrence of this lesion should be fairly common since estrogenic therapy for disseminated carcinoma of the prostate is practically a routine procedure." The implication of the above statement is that before estrogens can act as accelerating agents, the fundamental histological changes must have already been present.

Several interesting cases are reported in the literature. Howard and Grosjean[22] reported a case of "a man on whom a clinical diagnosis of carcinoma of the prostate with bone metastases was made on July 27, 1943. From this date until his death on January 4, 1948, he received a total of 40,280 mg. of diethylstilbestrol. At the time of death, bilateral scirrhous carcinoma of the breast was present." Abramson and Warshawsky[23] reported a case of unilateral breast malignancy in a male treated for prostatic carcinoma with 1,097 mg. of estrogens over 489 days. They pointed out in retrospect that the appearance of nodules in the breast should have suggested neoplasm. Entz[24] reported a case of what was thought to be metastases to the breast of prostatic carcinoma in a 49-year-old male being treated for 17 months with estrogens. He raises the question of whether or not estrogens actually enhanced the breast metastases and suggests that it would appear "advisable to treat the younger patients by castration rather than with estrogens."

Treatment: Castration is the only sure method of treatment, along with discontinuation of estrogen therapy. Treves, Abels, Woodard, and Farrow[25] describe the effects of castration on malignancy of the male breast. They came to the conclusion that about 50 per cent of the cases so treated show marked improvement and that malignancy so treated remains inactive for long periods.

CARCINOMA OF THE PROSTATE GLAND

In 1935, Kutscher and Wolbergs[26] isolated acid phosphatase and showed definitely that its origin was from the prostate gland and that it was active in acid solution only. In 1936, Gutman and Spraul[27] showed that the enzyme could be found only in the adult organ and not in the infant. They also were able to demonstrate the enzyme in malignancy of the prostate and in distant metastases. Huggins[28] in 1941 first showed the value of orchiectomy in inhibiting the growth of prostatic malignancy by research on dogs. Huggins[15] also demonstrated that "carcinoma of the prostate is most common in men between 40 and 90 years with the highest incidence at the ages of 60 to 70 years."

Chemical Patho-physiology: Huggins[28] was able to prove definitely the accelerating effect of testosterone on these tumors, and he showed that estrogens as well as orchiectomy were of value in inhibiting the growth of these tumors. Unfortunately, he also demonstrated that orchiectomy gave no more than temporary relief and was only palliative. The explanation for the failure of orchiectomy to entirely eliminate testosterone was interpreted on the basis of the remaining androgenic activity of the adrenal glands, which seemed to be stimulated following orchiectomy. Studies by Scott and Vermeulen[29] and later by Hug-

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gins and Scott[30] gave conclusive evidence that estrogens were of value in inhibiting the growth of prostatic carcinoma and of decreasing the 17-ketosteroids in the urine, showing that estrogens had effectively inhibited the secretions of androgens by the adrenal gland. This action has been explained by the inhibiting effect of estrogens upon the pituitary elaboration of gonadotropic hormone which stimulates the production of androgens by the adrenal gland. As Huggins states, "When stilbestrol is given, the urinary estrogens rise by virtue of the excretion of the administered drug, urinary gonadotropin levels fall, and androgen levels, as judged by urinary 17-ketosteroids, fall."

Nathanson[1] has demonstrated that castration and injection of estrogens produced little change in the acid phosphatase level if it is normal before therapy. Castration and injection of estrogens into patients with prostatic carcinoma having marked elevation of the acid phosphatase result in a sharp reduction of the level of the enzyme, but seldom to normal. Administration of androgens produces a sharp rise in the serum acid phosphatase.

Clinical Treatment: As has already been implied, three methods exist for a rational approach to the treatment of prostatic carcinoma. They are (1) orchiectomy, (2) administration of steroid hormones, and (3) adrenalectomy. All of the principles are based upon the already mentioned and well recognized fact, that testosterone is essential for the growth of prostatic carcinoma and metastases. The first method as devised by Huggins[28] was designed to abolish the primary source of testosterone production. The second method, as already stated, is based upon the assumption that estrogens will neutralize the effect of testosterone within the body or so depress the pituitary that the remaining source of testosterone (the adrenal gland) will be effectively inhibited. Thus, three methods are at hand for effective treatment. However, during the past ten years considerable controversy has arisen as to just how each should be used and the time of preference of one mode of therapy over the other.[32] As Nathanson[1] has shown, "Castration or hormonal therapy should not be resorted to in operable carcinoma of the prostate without metastases." He points out further, "Most patients who benefit from castration or estrogen therapy have recurrence of the signs and symptoms within a few years and many are not relieved for more than a few months."

Because the measures outlined have been shown to be only palliative in the majority of instances, this has been a source of disagreement as to what measures are indicated and at what time in the course of the disease. Huggins[15] is of the opinion that "if the lesion is confined to the prostate or nearly so, total prostatectomy by the perineal route is indicated; otherwise, for most patients, orchiectomy is advised as soon as the diagnosis of advanced cancer has been established." He stresses the belief that orchiectomy has yielded better results than treatment with estrogens.

Nathanson[20] has summarized the question as follows: "Some advocate combined orchiectomy and estrogen therapy, but there are inconclusive data to indicate that this has a definite advantage over either method. Orchiectomy is the preferred technic if the patient is unreliable or cannot tolerate estrogens. It is also the procedure of choice where immediate relief of symptoms is desirable, since estrogens may require several weeks to produce the same effect. Estrogens may be used in all other situations and certainly if the patient is disinclined to accept orchiectomy." He states further that "the optimum time to initiate therapy has not been established. Two theories are supported. One states that therapy should not be instituted as long as the patient is asymptomatic; that probably orchiectomy should be used first for immediate relief and that estrogens be given when there is a return of symptoms. The other theory points out that the above theory may have many pitfalls. First, it assumes that the malignant cells will not be less responsive to therapy after a few months than with the immediate diagnosis, or in fact that they may become more resistant. And furthermore, that orchiectomy and estrogen therapy should be given together, one enhancing and supporting the effects of the other. At present it is generally accepted that treatment should probably be withheld in asymptomatic cases. No conclusive statement can be given as to how therapy should be given once it is decided upon; that is whether to combine orchiectomy with estrogens or to start each separately." He further states that "castration may occasionally be of value following recrudescence of the disease after preliminary successful treatment with estrogens. The reversal of this sequence may also be of benefit in a few cases."

Nesbit and Cummings[31] believe that "it therefore would appear rational to delay the institution of endocrine therapy until pain and cachexia develops, for only by this means can the patient hope to derive the dual benefits of this treatment: prolongation of life by suppression of carcinogenic activity and relief of pain." They report further that in some cases pain may only be relieved by castration when stilbestrol has been administered previously.

Bumpus, Massey, and Nation[32] express their opinion, "Since all forms of therapy to date have proved only palliative, the prolongation of such treatment seems preferable to its immediate total application." They believe that each method should be used separately to afford the patient the greatest relief. They also believe (contrary to Huggins' opinion) that stilbestrol alone in small daily dosages is sufficient to

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control the disease, and they have reported three patients who remained well after over two years of treatment on stilbestrol alone.

Emmett and Greene[33] state that "bilateral orchiectomy is especially efficacious when the metastatic growths have given rise to symptoms." They further question whether "prophylactic" orchiectomy (done in the early stages of the disease before metastases have appeared) influences the course of the disease.

Alyea[34] states that "any malignancy should be attacked from the start with the most efficient therapy. The treatment which offers the best chance of success should be first. Therefore, orchiectomy should be carried out as soon as the diagnosis of carcinoma of the prostate is made. This will remove the major part of the androgenic hormone. Then the extragonadal androgenic hormone should be inactivated by diethylstilbestrol. This should be started immediately after operation. In this way, as soon as the gonadal hormone has been eliminated, the estrogen will be given to inactivate at once any extratesticular androgens which may be produced by the adrenals or other glands. By orchiectomy we know we are eliminating the greater part of the offending hormone. By estrogen therapy we think we are inactivating it, but how much of it?"

Crane and Rosenbloom[35] concluded from their studies that "the treatment of choice in carcinoma of the prostate is through transurethral resection, castration, and continuous administration of stilbestrol. This is essentially the opinion of Chase, Burt, and Hess[36] too.

Herger and Sauer[37] believe that "orchiectomy should not be carried out indiscriminately in all cases." They have used as a criteria the rapid enlargement of the primary lesion. They further state that "castration is the more effective procedure if quick relief from pain is the object of therapy." They warn that "combined treatment does not offer any advantage over castration alone." They also point out that orchiectomy following stilbestrol therapy may be followed by improvement while estrogen administration following failure of orchiectomy to relieve pain is almost always ineffective.

Clinical Results: As has been stated above, the only benefit that can be expected with the above mentioned methods (except in a few rare cases) is the palliative relief of symptoms. Again we find that treatment is not curative. Nathanson[1] has pointed out that "certain cases do not respond to treatment at all, whereas others show striking clinical improvement and relief of pain. Those lesions which more nearly resemble the adult gland seem to respond best to the therapy." He has also noted that serial biopsies of prostatic tumors "reveal marked degenerative changes in the cells when stilbestrol is given over a fairly long period of time."

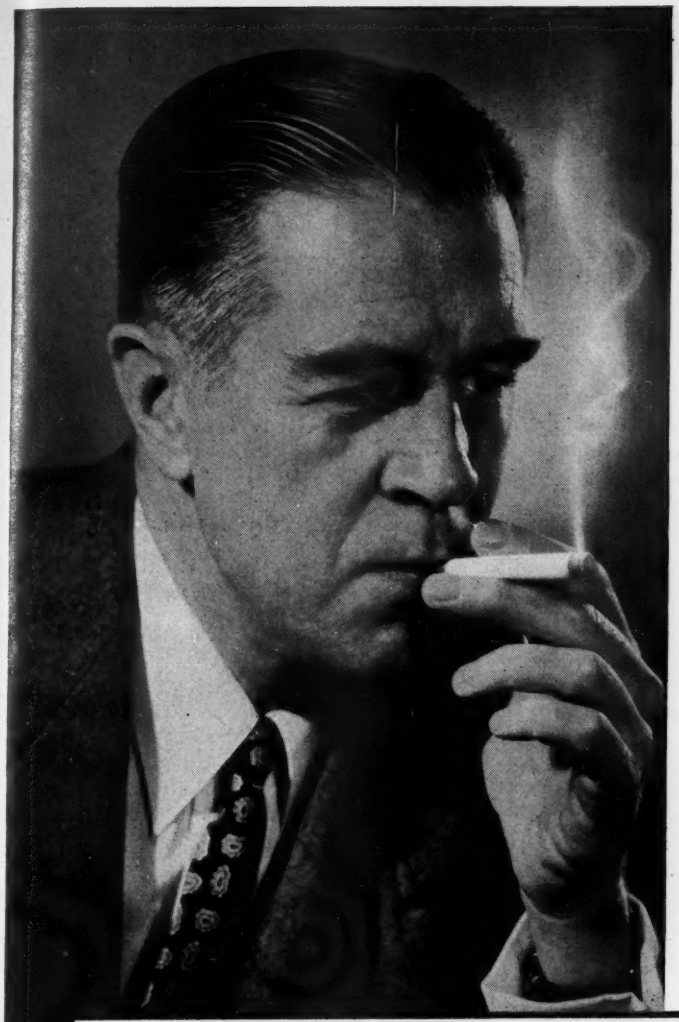
McCullagh[5] states that "it should be clearly understood that castration and later estrogens are to be used as palliative and not curative treatment. Estrogen therapy should never replace surgery in operative prostatic carcinoma." Huggins[15] is of the opinion that "antiandrogenic measures effect an improvement in the disease in about 90 per cent of patients treated by excision of the testes or by administration of estrogens."

Nesbit and Cummings,[31] reporting on 75 cases observed for at least 21 months following orchiectomy, have demonstrated "(1) early and satisfactory relief of pain, which occurs in from 20 to 72 hours in most instances, (2) generally good increases in weight, and (3) most patients experienced more normal urination following castration." They stated further that "orchiectomy provides only temporary suppression of neoplastic activity." Also, "endocrine therapy suppresses the neoplastic development of both early and advanced cases and in each instance it produces a corresponding prolongation of life, *but* it does not permanently retard the growth of the primary tumor nor does it prevent the occurrence and the eventual progression of metastases."

Crane and Rosenbloom[35] in a study of 340 cases felt that "(1) subjective improvement was present earliest when castration and/or estrogen was combined with transurethral resection, (2) when employed with transurethral resection, castration alone is more effective than estrogen alone; estrogen does not substitute for castration but only reinforces it, (3) transurethral resection combined with castration and estrogen (usually stilbestrol) produced the earliest subjective improvement and the longest median survival time in this series."

Herger and Sauer[37] in a study of 130 cases conclude that "it has been our experience that spread or local extension of bone metastases is not arrested as a rule by androgen control treatment. Such treatment does not ensure developing metastases at a future time." Scott and Benjamin[38] reporting on bilateral orchiectomy in 82 cases state that "most of the patients treated by this method were either dead or had lost its initial benefits within 36 months." These were also essentially the findings of Stirling.[39]

As pointed out by Huggins and Johnson[28] there are "two factors of significance in determining the effectiveness of orchiectomy: the tumor must be androgen dependent and the testes must contribute functionally significant amounts of the total production of androgen." Also, "the beneficial effects of estrogens in our experience have not been prolonged nor have we encountered any other agent which would greatly benefit in post-orchiectomy failure." Vest and Fraz-



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ier[40] in their studies have shown that the average expected survival time with adequate treatment in advanced prostatic carcinoma is from 18 to 33 months.

Undesirable Side Reactions of Stilbestrol: McCullagh[5] reports "the untoward effects of stilbestrol therapy in men include nausea, vomiting, and in some muscle pains and edema. Complete impotence is the rule; the nipples and areolae become dark, and a rather striking degree of gynecomastia appears." Huggins[15] has pointed out the danger of inducing carcinoma of the breast with stilbestrol therapy. He also has noted that "lactation is not too uncommonly observed."

SUMMARY

An attempt has been made to review the most recent advances in the hormonal therapy of carcinoma of the breast and prostate. Careful consideration of the side effects to be expected from hormonal therapy and the drugs and dosages of choice is presented. The use of caution and good judgment with adequate experience is cited.

While the results with hormonal therapy have proved to be only palliative and not curative to date, continued research in this field may yet lead to a more adequate and longer-lasting treatment for cancer. As Rhoads[41] has so ably remarked, "We have high hopes that we can so define the disturbances which lead to the precancerous changes in such patients as to allow us to name the chemical compounds lacking or produced in excess. We hope at the same time, on the basis of the knowledge developed of hormone manufacture in man, to be able to correct the abnormality when defined, before cancer has fully developed and when the abnormal tissue still can return to normal stages under treatment."

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The National Foundation for Infantile Paralysis has announced the approval of research and professional education projects totalling $2,586,271 for the period beginning in January, 1953. The awards go to 32 medical schools, hospitals, research institutions and educational organizations. Of the total authorized, $1,585,465 was allocated for research seeking prevention of the disease and improved methods of treatment; $1,000,806 was allocated for programs in professional education.

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ANNOUNCEMENTS

The 13th annual essay contest of the Mississippi Valley Medical Society will be held in 1953, with May 1 as the deadline for submitting entries. A cash prize of $100, a gold medal, and a certificate of award will be given for the best unpublished essay on any subject of general medical interest, including economics and education. Details of the contest may be secured from Harold Swanberg, M.D., Secretary, Mississippi Valley Medical Society, 209 W.C.U. Building, Quincy, Illinois.

Qualifying examinations for fellowship in the United States Section of the International College of Surgeons will be held at the Cook County Graduate School of Medicine and the Cook County Hospital, Chicago, on the following dates: May 4 and 5, August 10 and 11, and November 2 and 3. Applicants are asked to write Harry A. Oberhelman, M.D., Secretary, Qualification and Examination Council, 1516 Lake Shore Drive, Chicago 10, Illinois.

The annual meeting of the American Goiter Association will be held at the Drake Hotel, Chicago, on May 7, 8, and 9, 1953. The scientific program will deal with goitre and other diseases of the thyroid gland.

The First World Congress on Fertility and Sterility will be held May 25-31, 1953, at the Henry Hudson Hotel, New York City. It is sponsored by the International Fertility Association with the cooperation of the American Society for the Study of Sterility. Twenty-three scientific sessions will be conducted in English, French, and Spanish, with the use of earphones and simultaneous translations, as in United Nations meetings. Reservations are to be made with the chairman of the Local Arrangements Committee, 1160 Fifth Avenue, New York 29, New York.

The Southwest Allergy Forum will convene at the Hotel Muehlebach, Kansas City, Missouri, on June 14 and continue through June 16. Those interested in participating in the program, devoted to practical aspects of allergy, are asked to write the president, Orval Withers, M.D., Bryant Building, Kansas City 6, Missouri. Members of the local committee, in addition to Dr. Withers, are Dr. Cecil Kohn, Dr. R. Dale Dickson, Dr. Frederic Speer, Dr. Stanley Goldman, Dr. Ralph Hale, Dr. Herbert Rinkel, and Dr. Vernon C. Wiksten. Reservations should be made soon at the hotel; they may be cancelled later if necessary.

An advanced course in autoradiography and three basic courses in radioistotope techniques will be conducted at the Special Training Division of the Oak Ridge Institute of Nuclear Studies this spring and summer. The autoradiography course will be held from June 15 through June 25, and basic courses of four weeks duration will begin on June 8, July 6, and August 10.

Application forms and additional information may be obtained from the Special Training Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tennessee.

The Kansas Division of the American Cancer Society announces its 1953 contest for graduate students, interns, residents, and other scientific investigators. Prizes of $500, $300, and $100 will be given winners in two classifications, pre-doctorate and post-doctorate, for work done in fields related to the growth, cause, diagnosis, or treatment of cancer. Full information and application blanks may be secured from the office of the Kansas Division, 824 Tyler Street, Topeka.

Aid to Medical Education

Nearly 37,000 physicians contributed more than $3,150,000 in direct support of medical education last year. This total, however, does not include amounts given for buildings, endowments, scholarships, research and other special purposes. Dr. Donald G. Anderson, secretary of the A.M.A.'s Council on Medical Education and Hospitals, announced that reports from 76 of the country's 79 medical schools indicate that more than 29,000 doctors gave $2,258,534 directly for teaching budgets.

The American Medical Education Foundation raised $906,553 of the total from more than 7,000 individual contributors. The 1953 fund-raising drive has been launched with a third gift of $500,000 from the A.M.A. Since its organization two years ago, the foundation has raised more than two million dollars from the medical profession for distribution "without strings attached" to medical schools.

Basic research involving the connective tissue, the framework of the human body, will be emphasized in 15 medical centers throughout the country through grants made by the Arthritis and Rheumatism Foundation. Fellowships totalling $77,300 for research have been dispersed among 16 doctors specializing in rheumatic diseases.

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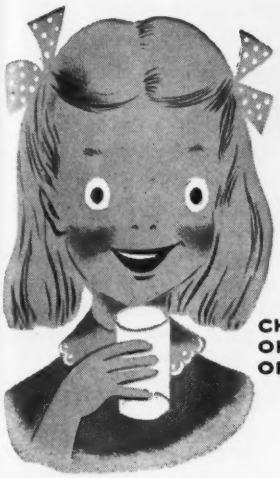

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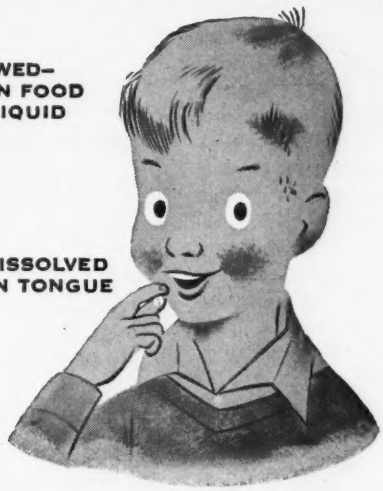

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BOOK REVIEWS

Standard Values in Blood. Edited by D. C. Albritton. Published by W. B. Saunders Company, Philadelphia. 199 pages. Price $4.50.

This compilation of data on the composition and reactions of blood was produced by a group of over 600 leading scientists, under the direction of the committee of the American Institute of Biological Sciences. This Institute is associated with the National Research Council as a part of the Council's Division of Biology and Agriculture. The book consists of tabular data concerning the normal levels of most of the constituents of blood in man and in many of the common experimental animals. In addition, several sections contain information about certain reactions of blood, such as blood clotting and changes in blood due to radiation and storage. Blood levels of some constituents during pregnancy and other non-pathological states are also included.

An outstanding feature of the tabulation is an attempt to furnish, along with the mean value and the range of values for a given constituent, an estimate of the reliability of that range. In as many cases as possible the range of a set of values is the "95 per cent range," that is, excludes the highest and lowest 2½ per cent of the data. This includes all the values falling within plus or minus two standard deviation units from the mean, and thus obviates the necessity of a calculation on the part of the reader to obtain the range from the standard deviation.

The book is divided into two sections, one containing the tabulated data, and the other the complete literature references from which the data were obtained. About one-third of the book is occupied by the bibliography.

The method of tabulating and labeling the data is, in some places, very intricate, but is probably necessary because of the large volume of material which is presented. The authors have been quite thorough both with regard to the types of blood constituents which were included and with regard to the data available to each type. In addition to all of the clinically important blood values, such information as levels of blood hormones, vitamins, and enzymes, as well as effective blood levels of therapeutic agents are included. A very satisfactory index was compiled by the authors.

The book will be of great value to medical and biological scientists interested in research involving blood constituents. It should save such an investigator many hours of arduous library work. It would not be of exceptional value to the average medical practitioner and was not so designed. All clinical laboratories of any size would very likely profit by having this book available.—*H. J. G.*

American Pocket Medical Dictionary. 19th edition. Published by W. B. Saunders Company, Philadelphia. 639 pages. Price $3.25 plain; $3.75 with thumb index.

This dictionary, published early in 1953, is a book which will find ready acceptance by physicians and those in related professions. It is not comprehensive, nor is it intended to be; it is offered as a quick reference work, an extra, for those who do not have immediate access to a more extensive dictionary.

In preparing the work, the editorial staff drew freely from the 22nd edition of the American Illustrated Medical Dictionary (Dorland), published in 1951 by the same company. That fact attests to the dependability of the volume, which will be of practical value to all in medical or scientific work. —*P. F.*

Nutrition and Diet in Health and Disease. Sixth Edition. By James S. Lester and William J. Darby. Published by W. B. Saunders Company, Philadelphia. 710 pages, supplementary tables of food composition. Price $10.

The new exchange method of calculating diabetic diets is a valuable addition to this volume. The discussion of the low sodium regimen and the rice diet has been revised. The section on atherosclerosis now includes a table of the cholesterol content of foods. The chapters on vitamins, the nutritional anemias, and the deficiency diseases have been rewritten. A table of the sodium and potassium content of foods and waters is useful to the physician and dietitian. The organization of the book is essentially the same as the earlier editions. It still remains a helpful reference.—*S.K.*

ABSTRACTS FROM CURRENT LITERATURE

Treatment of Amebiasis with Atabrine Combined with Carbarsone. By Ryle A. Radke, Ann. Int. Med., 34:6, 1432-1444, June, 1951.

The author reports a patient who was critically ill with amebiasis in whom a liver abscess had penetrated the diaphragm, and in whom a bronchopleural fistula was present. He had received two courses of 10 grs. of emetine in less than a month with no response. Since there had been evidence that atabrine had depressed amebiasis in some war areas, the author

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thought it might be worth trying in this case. After four days on usual dosages of atabrine the patient made an amazing improvement, the temperature became normal and sputum soon ceased.

Carbarsone seemed to be most effective in destroying amoebic cysts in vitro, so it was given to the patient for a 10-day period in dosage of 0.25 gms. two to three times daily. Atabrine was also given for a 10-day period in dosage 0.1 gm. three times daily.

Emetine is a dangerous drug, some finding complications in 91 per cent of cases. Electrocardiographic changes were found in 74 per cent of a series of 38 cases, usually significant changes in the T wave.

A relapse rate of 21 per cent was reported on cases treated with emetine intramuscularly, with emetine bismuth iodide, quinoxyl and stovarsol by mouth, 48 per cent relapse after emetine alone, 42 per cent after diodoquin alone, 26 per cent after combined emetine and diodoquin, and 44 per cent after combined emetine and carbarsone. The authors report a relapse rate of 12 per cent after combined atabrine and carbarsone treatment.

This 12 per cent relapse rate was determined after cases were followed for 60 to 395 days by means of smears and cultures of material taken from patients at recheck sigmoidoscopic examination. Severe reactions were encountered in two cases, one a dermatitis due to carbarsone, the other a toxic delirium due to atabrine.

Frequently repeated stool examinations were negative on amoebic suspect cases, the amoebae being found only by sigmoidoscopic examination, with aspiration of material from ulcers for study.

The author concludes that atabrine is an amebacidal agent which is relatively safe for use in the doses recommended.

It should be employed in conjunction with another amebacidal agent capable of eliminating the cysts of the organism.—*D.R.D.*

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Pacifiers for Infants

The Treatment of "Colic" in Infancy by the Use of the Pacifier. By Milton I. Levine and Anita I. Bell, Jnl. Ped., 37:5, 750-755, Nov., 1950.

The so-called "colic" baby has been a problem for all pediatricians. The parents develop a degree of anxiety that frequently influences the future emotional stability of the child. Nearly all of these infants are hypertonic, differing markedly from the relaxed and placid infant who nurses and sleeps with complete satisfaction.

It is generally accepted on the basis of experimental studies that an infant not only has a sucking reflex but, more than that, a sucking urge—a definite need for oral satisfaction. This need is entirely separate from the necessity of sucking as an adjunct to eating. This fact was pointed out originally by Freud, who placed emphasis on the importance of the oral zone, not only in the desire for feeding but in the desire for sucking as well. It has also been pointed out how children, when deprived of oral satisfaction, resort to thumbsucking as a substitute.

Twenty-eight infants with histories typical of colic were placed on pacifiers, and in every instance except two the pacifier was readily accepted. With the exception of three infants, the pacifier was successful in relieving the irritability and crying of the infant and in causing a cessation of the symptoms of "colic." The use of the pacifier does not form a habit; the children discarded it spontaneously at an average age of 13.8 months. In only two of the 28 cases did the infants resort to thumbsucking during or after discontinuing the pacifier, and these two only while going to sleep after the pacifier had been discarded. The fact that certain crying infants do not respond to the pacifier by relaxation would lead to the conclusion that their difficulty was probably due to an etiological factor unrelated to the need for sucking.—*D.R.D.*

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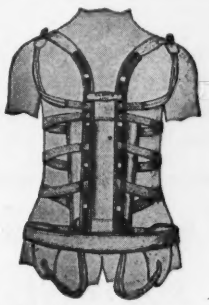

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Gallbladder Surgery, Ten Hours, starting April 20
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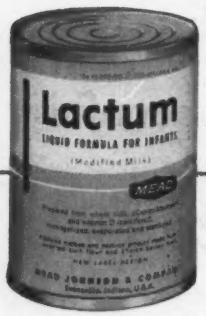
1. Frost, L. H., and Jackson, R. L.: J. Pediat. 39: 585-592, 1951.



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